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CONTENTS

	PAGE
NOTES ON THE FALLING REFLEX OF CATS. *Henry R. Muller and Lewis H. Weed*	373
THE CIRCULATION OF THE BLOOD IN MAN AT HIGH ALTITUDES. III. THE EFFECTS OF PHYSICAL EXERTION ON THE PULSE RATE, ARTERIAL, AND VENOUS PRESSURES. *Edward C. Schneider, assisted by Glen E. Cheley and Dwight L. Sisco*	380
THE APPEARANCE OF SUGAR IN THE SECRETIONS OF THE DIGESTIVE TRACT FOLLOWING THE ADMINISTRATION OF PHLORHIZIN. *R. G. Pearce*	418
THE DESTRUCTION OF HORMONES, PROENZYMES AND ENZYMES BY ULTRA-VIOLET RADIATION. *W. E. Burge, W. R. Fischer, and A. J. Neill*	426
A NOTE ON THE EXCITATION OF THE PHRENIC NERVE BY THE ACTION CURRENT OF THE HEART. *F. H. Pike*	433
THE CHARACTER OF THE INNERVATION OF THE KIDNEY. *Russell Burton-Opitz*	437
SOME OF THE GENERAL PHYSIOLOGICAL PROPERTIES OF DIAPHRAGM MUSCLE AS COMPARED WITH CERTAIN OTHER MAMMALIAN MUSCLES. *Frederic S. Lee, A. E. Guenther, and Henry E. Meleney*	446
SOME OF THE CHEMICAL PROPERTIES OF CERTAIN MAMMALIAN MUSCLES. *Frederic S. Lee, Ernest L. Scott and W. P. Colvin*	474
THE REACTION OF TEMPERATURE AND HUMIDITY ON THE WORKING POWER OF MUSCLES AND ON THE SUGAR OF THE BLOOD. *Frederic S. Lee and Ernest L. Scott*	486

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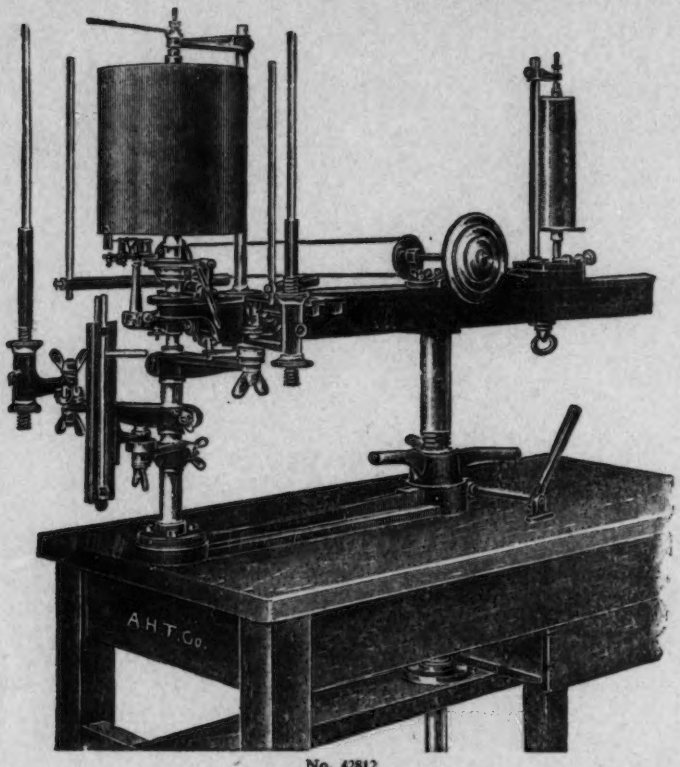

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NOTES ON THE FALLING REFLEX OF CATS

HENRY R. MULLER AND LEWIS H. WEED

From the Anatomical Laboratory of the Johns Hopkins University

Received for publication February 23, 1916

The ability of cats to turn in the air and to land squarely upon their four feet when falling is a very well known and interesting phenomenon. This response to falling is found invariably among normal cats; the rotation in the air occurs to either side dependent only upon the initial position in the air. Thus a cat with its legs inclining more to the right will turn to this side, making the subsequent rotation more easily. The reaction is so typical and inevitable that it seemed to offer an opportunity to test the hypothesis that many of the phenomena obtained in decerebrate animals were the result of an antigravitational tendency in the lower centers of the nervous system. This view-point was first advanced by Sherrington (7) who stated (p. 302) in regard to the rigidity following decerebration:

> The muscles it predominantly affects are those which in that attitude antagonize gravity. In standing, walking, running, the limbs would sink under the body's weight but for contraction of the extensors of the hip, knee, ankle, shoulder, elbow; the head would hang but for the retractors of the neck; the tail and jaw would drop but for their elevator muscles. These muscles counteract a force (gravity) that continually threatens to upset the natural posture. The force acts continuously and the muscles exhibit continued action, tonus.

The importance and significance of such an hypothesis seem to us to warrant further investigation. A search through the available literature failed to reveal any studies of the matter in animals which exhibited characteristic antigravitational reactions. Likewise no record could be obtained of any physiologic analysis of the factors involved in this typical rotation of cats when falling, although the physical aspects of this

phenomenon have been more or less extensively investigated. In addition it was felt of value to ascertain the physiological anatomy of this response to falling—what pathways are involved, what anatomical structures yield the initial stimuli, and what influence the cerebral cortex has in the process.

The results of the experiments here reported have been, in the main, so consistent, that it seems pardonable to present them even though the series be small. All of the observations were made as acute experiments, allowing the cats to recover wholly from the anesthesia before testing the responses. These acute experiments were employed to avoid any possible assumption of function by other organs, to compensate for the experimental procedures. The animals were dropped varying distances upon a soft bed of straw in order that no discomfort could be caused by any failure of the normal rotation. For the routine observation the animals were held in a horizontal position, with their backs to the floor, and an effort was made to avoid imparting to the animal any rotatory impulse on releasing the hands.

A study was first made of this turning or falling reflex in normal cats. All of these animals invariably, when dropped, turned in the air so as to fall easily upon the feet. The turn in the air occurred almost immediately after the support was removed, the rotation being in the direction of the greater ease. All of these normal animals were able to complete the turn perfectly within a fall of 1 foot; some were able to accomplish the same twist of the body within the surprisingly short distance of 6 inches. When these normal animals were blinded with a tightly fitting mask, the rotation was made almost as perfectly and as quickly as by the normal animal. The landing upon the straw was, however, not as accurate in these masked animals, seemingly because of their ignorance as to the height of the fall.

The reflex rotation of these blinded cats in the air suggested immediately that the semicircular canals were the source of the initial impulse which occasioned the motor response. Hence, under full anesthesia, these canals were destroyed by an extra-cranial route—first on one side and subsequently upon the other. It was found possible to accomplish this destruction of the internal ear completely by this method without affecting neighboring structures.

If in a normal cat, the three semicircular canals on one side be destroyed, there will result a marked horizontal nystagmus to the opposite side, a partial rotation of the head away from the lesion, and a variable degree of ataxia (especially in the head). The animals strongly resist

rotation away from the lesion, reclining always upon the operated side. Ewald (3), Cyon (2), von Stein (8) and others have described such acute symptoms for several other species. Somewhat similar acute disturbances were found by Lee (5) in the case of the dog-fish, after cutting the acoustic nerve—deflection of the eyeballs, change of position of the fins, curving of the body to the operated side and reclining upon this side.

When, however, one of these experimental cats with a unilateral lesion of its semicircular canals was dropped, it was always found, in this series, to rotate in the air, and to land upon the straw in a fairly normal fashion. The motor response in this rotation was never as perfect as in the normal cat, due possibly to the removal of some vestibular influence upon the muscular tonicity (Ewald). In addition, the animals usually required a greater distance in which to inaugurate their rotational movement.

Bilateral loss of the vestibular apparatus altered markedly the muscular, postural and ocular reactions of these cats. These animals exhibited no nystagmus of any character; the ataxia was frequently tremendously augmented; no preference was shown for either side on lying down. These changes in the reactions of the animal were particularly well shown in these observations when the experimental procedure was of two stages: in the first operation, the canals on one side were customarily destroyed with a resulting ataxia, nystagmus away from the lesion and a definite tendency to recline only on the operated side; after the loss of the second canal-system, the ocular and postural reactions disappeared with an accentuation of the ataxia.

Quite similar to our findings in the unilateral lesions were the reactions on falling shown by animals with both internal ears destroyed. Such cats, after complete recovery from the anesthesia, on being dropped, will turn in the air and land upon their feet. This result, at variance with our preconceived notions of the process, has been repeatedly found in every one of the animals observed.

But apart from the inevitable ataxia in the turning movement of the animals with one or both of their canalicular systems destroyed, there was found in these experiments a marked difference in the response of animals in which one internal ear or both internal ears had been destroyed. The animals with a unilateral loss of the semicircular canals were observed, on falling, to turn always away from the lesion. In other words, such an animal with the right internal ear destroyed, would inevitably twist in the air to the left, even though this necessitated a rotation of the body through 270 degrees. On the other hand,

the destruction of both of the canal-systems permitted the animal to rotate in either direction (this being determined apparently by the angle to be traversed in the rotation).

Such findings inevitably force one to assume that other organs than the semicircular canals are able to initiate this falling reflex in cats. This other receptor which occasions the reflex seems to concern the eyes. If, as stated above, a normal cat be blinded, the falling reflex occurs as in the unblinded animal. But if these animals in which one or both of the semicircular systems have been destroyed, are blinded by the hood, no rotation will take place on falling. This finding was wholly constant in our series of animals in which both internal ears were destroyed; it was constant in a small majority of cases, in those animals in which only one canal-system was removed. The results, here, indicate that either the vestibular or optic systems may serve as the receptor organ for the rotation on falling; either of the two systems is sufficient to inaugurate the reflex, but if both are deprived of function, the turning reflex will not take place. The failure of blinded cats with one intact vestibular system to rotate is probably to be explained on the basis of a disturbed vestibular equilibrium; these animals are afraid or unable to trust, with one internal ear but recently destroyed, the impulses derived from the intact vestibule. Certain of these cats with unilateral loss of the semicircular apparatus will turn in the air when blinded; the rotation occurs, as in the unblinded animals, away from the lesion. It seems most likely that these animals learn more quickly than the others to place a certain reliance upon the stimuli coming from the intact canals.

Based on this evidence, the most logical interpretation seemed to be that both the eyes and the semicircular canals were able to give rise to impulses on falling that resulted in the rotation of the cat in the air. It is difficult to ascribe any greater importance to either of these organs; either seems wholly capable of initiating the same reaction. Probably both the ocular and vestibular mechanisms are normally employed in such a fall.

The physiological anatomy of the reflex on this basis seems fairly well established on its afferent side but not at all on its efferent pathway. Naturally one of the first questions to be solved here would concern the possible use of the pyramidal tract as the motor bundle. This was determined experimentally by testing the falling reaction of cats in which the motor cortex was ablated on one or both sides. Such a procedure would remove the connections of the pyramidal cells from

their effectors, rendering it impossible for the animal to employ this cortico-spinal fasciculus. In these extirpations the motor cortex was often delimited by unipolar faradization; the ablations were always extensive, involving a considerable portion of the anterior half of the cerebral hemisphere. On recovery from the anesthesia, these animals rapidly acquired the power of locomotion and also of other purposeful movements—a finding to be expected in view of the observations of Brown and Sherrington (1) on the chimpanzee.

Cats with unilateral ablations of the motor cortex on dropping showed a wholly normal ability to rotate in the air and land upon their feet. That this reaction was not due to a bilateral control over the body-musculature exerted by the remaining motor cortex was demonstrated by the bilateral ablations. Most of these animals turned, on falling, with a very perfect adjustment to land upon their feet. A single animal in this series, with bilateral motor ablations, was able to turn only its front legs, the posterior part of the body not participating in the necessary rotation. This observation was of interest in view of the work of Marey (6) who, by means of photography, was able to demonstrate that the rotation of a cat in the air was a two-fold process—in the first phase the front legs were carried around and in the second, the posterior part of the body underwent the same rotation.

On being blinded, cats with this unilateral extirpation of the motor area were able, on falling, to twist in the air and to land as perfectly as the normal animal. But with a similar bilateral lesion, the blinded animals did not show such consistent reactions. Some of these animals were able to turn in the air on falling; others rotated only at times, falling the rest of the time without muscular reaction. Still others required tossing upon the straw in such a way as to introduce lateral motion into the spatial senses. The explanation of these varying results cannot be here given; it would appear that the extensive cortical lesion had interfered somewhat with the afferent pathways, necessitating for the rotational response stimuli from both ocular and vestibular mechanisms, in great strength. Thus, the added excitation, introduced by the lateral movements, might break through the thresholds and occasion the typical motor response.

The exclusion, by the observations just recorded, of a necessary participation of the pyramidal path in the motor response to falling, naturally led to further delimitation in this rather typical antigravitational response. The next observations were made on cats with both cerebral hemispheres entirely removed. These animals on recovery

from ether were able to make progressive movements with both fore and hind legs, with no apparent excitation. Quite similarly coordinated movements could be obtained by appropriate stimulation. The optic nerves were undisturbed (reflex constriction of the pupil being elicited) as were also the semicircular canals. From these animals, however, no rotational reactions to falling could be elicited; the drops were not accompanied by any movements at all. This indicated that the cerebral hemispheres (consciousness?) were essential for the performance of this typical antigravitational rotation of cats.

Quite similar to these findings were the results of the observations made upon decerebrate cats. These preparations possess intact vestibular and auditory mechanisms (cf. Forbes and Sherrington (4)), with likewise intact rubro-spinal tracts. None of these decerebrate cats showed any tendency to turn in the air to avoid falling on their backs. And yet, these animals are able to make purposeful movements (as the scratch reflex) on proper excitation. As recorded previously by one of us (Weed (9)) destruction of the semicircular canals on both sides does not affect the existent rigidity. In these observations, the same failure to affect the rigidity was found on destruction of the canals on both sides; similarly, a previous bilateral destruction of the vestibular mechanism does not interfere in any way with the development of the typical decerebrate rigidity.

From these observations, then, a few conclusions may be drawn. The rotation of cats on falling seems to depend on excitations derived either from the eyes or from the semicircular canals. Loss of either of these organs of initial spatial relationship does not interfere with the falling reflex, but deprivation of both of these sensory fields abolishes this reflex. This rotational reaction also seems dependent upon some cortical influence (consciousness?) although it occurs after ablation of both motor areas. Decorticated (without cerebral hemispheres) and decerebrated animals do not, in our experience, show the slightest tendency toward rotation in the air. The rotation may be accomplished by the cat when deprived of the pyramidal tract by extirpation of the motor cortex.

Whether this rather typical reflex in cats, aroused by falling, may be considered an essential antigravitational reaction, would depend on many factors. The results here recorded surely offer no evidence either for or against the hypothesis that the muscular reactions in decerebrate rigidity are the result of an attempted resistance of gravity. The extensor thrusts of these animals, as pointed out by Sherrington

(7), surely suggest an effort to overcome gravity. But such decerebrated cats as here described, show no tendency to protect themselves against falling by means of the normal rotational movements. Hence it may be assumed that the falling reflex is probably an acquired form of protective mechanism, dependent on influences from the semicircular canals and from the eyes, mediated largely, if not entirely, through the cerebral cortex.

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THE CIRCULATION OF THE BLOOD IN MAN AT HIGH ALTITUDES

III. The Effects of Physical Exertion on the Pulse Rate, Arterial, and Venous Pressures

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In our earlier studies of the circulation at a high altitude (1) we dealt with men who were comparatively inactive muscularly. In these men a marked increase in the rate of blood flow was found to occur with residence at the high altitude and this was associated in part with an augmented rate of the heart beat and a fall in the venous pressure, and in part with a dilatation of the arterioles. Kuhn (2) also has demonstrated by calculations made from determinations of the oxygen capacity of the blood, the total oxygen consumption, and the pulse rate, that the heart responds to the influence of lowered barometric pressure by increasing its output per minute.

In the present paper the immediate and after effects of various forms of exercise upon the arterial and venous pressures and on the heart rate will be considered. The data have in large part been collected in Colorado Springs and during two expeditions to the summit of Pike's Peak. Five subjects served in the first expedition, three of the men went up by railway train and were on the mountain fourteen days, June 16–29, 1914, while the other two walked up and remained five days. In the second expedition two men went up by train and remained three and a half days in October 1915. In as far as was possible the exercises used were the same at the two altitudes, 6000 and 14,109 feet.

The exercises considered were walks of fifteen minutes duration at the rates of three and four miles an hour, short rapid runs, work on a stationary bicycle, leg raising, and walking up Pike's Peak. The walks at three and four miles per hour were made indoors on smooth

floors. It was impossible to secure comparable conditions at the two altitudes for the short runs therefore we had the men run as fast as they could in equal intervals of time.

THE PULSE RATE DURING REST

The early morning rate. Of all the circulatory changes due to diminished barometric pressure the acceleration of the heart rate is the most noticeable. In our recent expeditions to the summit of Pike's Peak we have continued the study of the early morning pulse rate in order to obtain a clearer understanding of the influence of muscular exertion and of mountain sickness on the heart. These counts were ma 'e on subjects in bed just after awakening. We have reported some of these data (1) and will now compare them with those of the recent expeditions. In our earlier report it was shown that the early morning pulse rate in men who were well and leading a sedentary life required several days after the ascent to reach its maximum rate. But in men who were mountain sick the rate was greatly augmented by the first morning and it thereafter retarded for several days. The data now presented cover observations on eight subjects, three of these men were studied during three and four trips and the others during a single sojourn. Five of the men have made the ascent on foot while one of these also went up twice by railway car.

For the men who ascended passively by train and were not mountain sick the rate, as found in our earlier work, was only slightly accelerated by the first morning and reached its maximum some days later. Sisco was healthy in two expeditions but had a slight bronchitis during a third. When well, in sojourn I, his heart rate on the first morning after the ascent had accelerated 4.5 per cent and by the fourth morning had advanced to 18.8 per cent; in sojourn III, by the first morning his pulse rate had increased 5.6 per cent and the maximum, 24.1 per cent, occurred on the third morning; while in expedition II when he was unwell, the pulse rate accelerated as much as 23.1 per cent by the first morning, the maximum, 28.8 per cent, occurred on the second morning. Schneider is always more or less mountain sick when he first goes to the summit of Pike's Peak. In expedition III, however, he was only slightly affected by the altitude, with the result that his pulse rate was up only 15.6 per cent the first morning after the ascent, the maximum rate, 21.9 per cent, was reached on the fourth morning. During the sojourns of more severe attacks of mountain sickness the

maximum rate occurred on the first morning, thus in expedition I it reached 46.6, in II 42, and in IV 22.4 per cent. He was less ill in IV than in I and II. In the three expeditions in which Schneider was mountain sick the maxima exceeded the maximum for the trip when he remained comparatively well. Cheley, who was a member of expedition IV, suffered with a headache the first night and had his maximum acceleration, 22.4 per cent, the first morning. Havens ascended in expeditions I and III passively by train, but walked to the summit in II. Following passive ascent his pulse rate increased 7.1 and 7.4 per cent respectively by the first morning and reached the maximum, 21.4 and 18.5 per cent respectively, on the fifth day in each. Following the exertion of climbing the mountain his pulse rate reached its maximum acceleration of 26 per cent by the first morning.

European workers have generally found the increase in the heart rate on the first morning of a sojourn at altitudes above 14,000 feet greater than we have reported. Thus Durig and Kolmer (3) in their expedition to Monte Rosa obtained the following: Durig from an average at low altitudes of 61 had advanced to 80 or 31.1 per cent, Reichel from 64 to 92 or 43.8 per cent, Kolmer from 58 to 89 or 53.4 per cent, and Rainer from 56 to 97 or 74 per cent. A further acceleration occurred for from one to three days in three of the men. These data were obtained on men who had undergone considerable physical exertion in climbing the mountain. Our observations on men who walked up Pike's Peak indicate that the greater per cent of increase noted by Durig and Kolmer must be attributed to the influence of the fatigue of the climb. We found that men who climbed the mountain reacted very like those who became mountain sick.

Atwater, Eager, Gregg, Havens, and Munro climbed Pike's Peak on foot. Atwater and Havens were in better physical condition than the others. Atwater had prior to the trip been working regularly out of doors as a house painter. Havens trained for the two-mile run and was in excellent condition. Atwater's pulse rate had advanced the morning after the ascent from 47 to 78 or 66 per cent, Eager's from 66 to 90 or 36.4 per cent, Gregg's from 57 to 73 or 28.1 per cent, Havens from 54 to 68 or 26 per cent, and Munro from 44 to 72 or 63.6 per cent. Atwater, Eager, and Havens reached their maxima the first morning while Gregg and Munro each reached the maximum on the second morning. Gregg's greatest increase was 33.3 per cent and Munro's 90.9 per cent. The amount of acceleration in the heart rate of our subjects who underwent the exertion of climbing the mountain varied

between 26 and 66 per cent on the first morning, while for Durig and Kolmer's subjects it ranged from 31 to 74 per cent. Contrast these figures with those of our subjects who ascended passively by train, and were not mountain sick, in which the pulse had only increased from 4.5 to 15.6 per cent on the first morning. On the other hand our subjects who were mountain sick showed on the first morning of residence accelerations varying betwen 22.4 and 46.6 per cent; these correspond more nearly with those of the group who underwent the physical exertion of the climb than with those who were well and ascended passively.

In not one of our subjects did the pulse rate during the stay at the high altitude wholly return to his Colorado Springs normal. Cheley's pulse rate made a remarkable return in his short stay on the Peak. His early morning pulse rate in Colorado Springs varied between 44 and 54 but was usually nearer the lower figure. On the third morning it was down to 50. Havens, Schneider, and Sisco remained two weeks on Pike's Peak in the summer of 1914. Havens' rate varied in Colorado Springs between 51 and 56. The thirteenth morning he had a rate of 56, lower by two beats than in any other sojourn on the Peak. Schneider's rate in Colorado Springs varied between 60 and 67, his lowest early morning count on the Peak was 72. Sisco with a low altitude rate varying between 50 and 57 was as low as 56 on only one morning, the tenth spent on the Peak. These indicate that in some men longer residence at the high altitude might restore the low altitude early morning rate.

The influence of posture on the frequency of the pulse. It is well known that the heart beat is influenced by posture. At low altitudes, and also at 6000 feet, when the body is changed from the reclining to the sitting and then to the standing position the beat will vary as follows: from 66 to 71 to 81 on the average.

It has been claimed that at high altitudes the variations in rate due to postural changes are greater than at low altitudes. Thus Zuntz and coworkers (4) found the frequency for one subject while reclining to be 80 and sitting 92, 106, and 108; another reclining 66, sitting 96, and standing 109; while a third subject gave reclining 84 and sitting 100. Fuchs (5) likewise emphasized the fact that the percentage of change in the three postures was much greater on Monte Rosa.

In a former paper (1) we showed that the early morning pulse rate, with the subject still in bed, and the rate throughout the day, when in the sitting posture, gave approximately the same percentage of increase on Pike's Peak as at lower altitudes. The heart was shown

to take a higher daily tempo and in general to vary proportionately around the new level.

During our last expeditions to the summit of the Peak the conditions for the study of the daily average of the pulse rate of subjects in the sitting posture were not as good as in the first expedition, which was the basis for our earlier report. It should be noted that in our recent expeditions each subject had daily to undergo a considerable amount of physical exertion. In a rough way the curves for the mean rate of the pulse for the sitting posture follow those of the early morning. This parallel condition of the two curves is most marked during the early days of residence on the mountain. In Sisco, during the expedition of longer residence, the daily mean remained high after the fifth day while the early morning rate showed a decline. He showed a remarkable decline in the mean rate the last two days of his stay. Havens' sitting rate followed the morning rate more closely but shows greater variation than Sisco's. His mean sitting rate fell the last days more decidedly than the early morning rate. Schneider's daily mean for the sitting posture remained rather constant throughout the entire stay as did his early morning rate. The retardation after ten days of residence noted in Havens and Sisco is similar to that observed by Douglas, Haldane, Henderson, and Schneider (6) in three of their subjects at the end of two weeks of residence.

A comparison of the mean pulse rates for the sitting posture in the three groups, the well carried up passively, the mountain sick who also went up by train, and those fatigued by climbing the Peak, brings out the same differences noted for the early morning counts. For those who ascended by train and remained well the percentage of increase in the mean on the second day, or the day following the first night spent on the Peak, over the Colorado Springs average varied between 4 and 15 per cent. In the mountain sick group the acceleration ranged from 23 to 33 per cent. Among those who walked up the mountain the increase in the mean rate on the second day ranged between 18 and 44 per cent. Three of the men who walked up the Peak had on the second day a mean rate of 105, 101, and 100. These men showed a retardation each succeeding day. The other two showed the highest mean on the third day and this also was the day on which the early morning rate was greatest.

Our records do not show the range of variation throughout the day among those fatigued by the climb to be greater than for the men who ascended passively. Eager's heart rate ranged on the second day

from 96 to 114, on the third from 84 to 110, on the fourth from 80 to 112, and on the fifth from 80 to 106. Munro gave the following: second day 81 to 106, third 94 to 108, fourth 80 to 96, and fifth 80 to 100. Others gave similar records. On contrasting these data with those tabulated by Schneider and Sisco for men who did not undergo great physical exertion we find the percentage range no greater. The maximum range of daily variation in the pulse rate among the men who climbed the mountain, during the five following days, was 40 per cent. The daily variation among the men of our former study ranged between 28 and 53 per cent which was not a greater variation than we found to occur in the same men at lower altitudes.

Havens, it will be recalled, ascended the mountain by railway train twice and walked up once. For the first three days following passive ascent the daily mean heart rate was 73, 82, 80 and 78, 79, 82 respectively, while for the three days after walking up it was 87, 96, and 86. The heart, therefore, takes at the high altitude a high tempo at once as a result of the fatigue of excessive exertion in climbing the mountain, but only gradually increases its rate when under the influence of reduced barometric pressure alone.

An exceptionally slow pulse rate was noted in Atwater the day after he made the climb to the summit. On that day his pulse varied between 72 and 84 with a mean of 78 which was only 18.2 per cent above his Colorado Springs average. The next day his heart was more irritable and advanced to a mean of 90 which was 36.3 per cent above his low altitude average.

Fuchs (5) in a series of observations upon himself found the acceleration of the pulse rate, in the standing posture as compared with that while reclining, varied at Erlangen between 8.6 and 11.7 per cent; while at Capanna Margherita on Monte Rosa the acceleration rose to 27.3 per cent. During our last stay on Pike's Peak the changes in the frequency of the pulse were determined in the morning before dressing and in the evening upon retiring for the three postures, reclining, sitting, and standing. Repeated counts were made extending over half minute and minute intervals and the particular position was kept for from three to ten minutes or until the pulse rate remained constant. Both subjects of this study were somewhat mountain sick the first night. Cheley, however, while awakening the next morning with a slight headache recovered completely after getting up. Schneider did not wholly recover until the following day.

Cheley's early morning changes were greater on Pike's Peak than in

Colorado Springs. The first morning no difference could be obtained between sitting and standing, and the total acceleration following the change from the reclining to standing position was then 12 beats. The next two mornings the difference between the reclining and standing positions was 22 and 20 beats. For the same positions in Colorado Springs the difference was in general 14 beats. The increase for the two postures on Pike's Peak varied between 20 and 42 per cent and in Colorado Springs ranged between 19 and 33 per cent. For Schneider the early morning variations due to changes in posture were about the same at the two altitudes. The total difference in the number of beats for reclining and standing postures on Pike's Peak for the three mornings was 21, 19 and 15 respectively and in Colorado Springs ranged between 15 and 19. The percentage of change on Pike's Peak varied between 20 and 25 and in Colorado Springs between 25 and 29.

The evening counts reveal some additional facts. In Cheley the differences in the number of beats for the reclining and standing postures when on Pike's Peak were less than those found in the early morning. For the three days the evening differences were 15, 17, and 13, a variation of from 19 to 26 per cent. In Colorado Springs the evening variations ranged between 6 and 17 beats or between 13 and 31 per cent. Schneider's reaction to changes in posture in the evening on Pike's Peak ranged between 13 and 28 per cent and in Colorado Springs between 13 and 27 per cent. Altitude differences in the amount of variation in heart beats were, therefore, clearly lacking in Schneider, while the postural differences for Cheley were only greater in the morning.

From our data on the influence of posture upon pulse rate it is evident that the heart is not necessarily more irritable to changes in body position at high than at low altitudes. In general it may be said that the heart works at an increased tempo in all postures at the high altitude. The height of the new level of heart rate differs with individuals. Some men show only a few beats of acceleration over the lower altitude, while some show an increase of ten and more beats per minute. An occasional subject may have a lessened rate as was the case with Haldane of the English-American Pike's Peak Expedition (6).

THE INFLUENCE OF PHYSICAL EXERTION UPON THE PULSE RATE

In the past a considerable number of observations have been made on the influence of high altitudes upon the heart rate during physical exertion. We have attempted in our study by the use of graded exer-

cises to analyze this influence somewhat more fully than previous workers. At very high altitudes all investigators have found that a more marked increase in the pulse rate occurs during work than with the same exertion at low altitudes. Veraguth (4) reported that in Zürich the ascent of a stairs of 50 steps increased his pulse 32.4 beats and in St. Moritz during the first ten days of residence 47.3 beats. Mosso (7) had several of his soldiers raise a pair of 5 K. dumb bells once every four seconds. One soldier raised them 121 times in Turin, as a result the pulse rate rose from 62 to 68 while on Monte Rosa after raising the dumb-bells 119 times the rate rose from 94 to 120. Kronecker (8), Zuntz and coworkers (4), and Durig (3) have studied such changes in greater detail. Stern (9) in 1913 made a still more exhaustive study. He corroborated the greater high altitude increase in frequency observed by others and noted that the curve describing the fall in the pulse rate after exertion always had a secondary ascent, while at low altitudes it was a smooth curve. Durig and Kolmer (3) were of the opinion that the amount of pulse rate increase could only partially be explained by the physical powers of the person under observation. The degree of acceleration was nevertheless influenced by training and adaptation. They also found that the after effects of exercise lasted a longer time in the mountain sick.

Just what height must be reached before altitude accentuates the exercise pulse rate has not been determined but Durig and Kolmer were convinced that at 6000 feet there was no noticeable influence. Our own experience in Colorado Springs definitely confirms this conclusion.

A. The after effects of muscular work on the pulse rate

Bowen (10) from a low altitude study of the changes in heart rate resulting from bicycling found that when work ceased there was a sudden and primary fall in the pulse rate, followed by a slower secondary fall, the two being frequently separated by a period of stationary rate—a plateau. Lowsley (11) reported that after short periods of exertion the pulse rate usually goes subnormal, but after fatiguing and exhausting exercises the pulse rate returns to normal more slowly and only rarely passes into the subnormal stage.

Walks at the rate of three miles an hour for fifteen minutes. The influence of the high altitude on the reaction of the heart to the very moderate and easy exercise of walking at the rate of three miles per hour for fifteen minutes was definite only during the first few days

of residence. Cheley after walking at this rate in Colorado Springs had on the average a 16 per cent acceleration in the heart rate, furthermore the heart returned to its normal rate by a uniform fall in from two to five minutes. The first afternoon spent on Pike's Peak the same exercise increased the heart rate from 86 to 120 or 40 per cent; this was followed by a rapid primary fall and then by a slower secondary fall which carried it down to 90 in six minutes, where it remained for twenty-two minutes. After this it again slowly dropped and was back to normal within the hour. The next morning the same walk raised the pulse rate 42 per cent, from 72 to 102 beats. It retarded rapidly to 90 where it remained for ten minutes and then gradually went down to 76 where it remained for more than an hour. The third day the acceleration was from 75 to 108 or 44 per cent. The rate returned to 81 in six minutes and then went up to 84 where it remained ten minutes, afterward it went subnormal. On the fourth and last day this walk caused an increase in the heart rate of 34 per cent, but the return to normal was quickly made, occurring in seven minutes which was nearly as rapidly as in Colorado Springs.

During the 1914 expedition Schneider walked twice for fifteen minutes at the three-mile per hour rate. The first time was on the second day spent on the Peak. His acceleration was then from 90 to 120 or 33 per cent. The return was gradual but slow. Eleven days later a similar walk increased the pulse from 94 to 102 beats or 9 per cent and the return to normal was completed within eight minutes. Schneider's average increase in Colorado Springs for this walk is 15 per cent and the heart rate returns to normal in from three to seven minutes. In the 1915 expedition Schneider's reaction to this amount of work was followed more in detail. The first afternoon the walk accelerated his pulse rate from 82 to 132, or 60 per cent. The rate fell to 90 in six minutes where it remained for fourteen minutes, it next went down to 88 and was there over an hour later. The second day this amount of work increased the pulse rate from 102 to 132 or 29 per cent, it fell to 101 in ten minutes and then returned to 104 where it remained for thirty minutes. On the third day the acceleration was 30 per cent, but the heart rate returned to normal within fifteen minutes. On the fourth day the acceleration was only 20 per cent and the return to normal occurred within five minutes. The reaction on this fourth day was a marked improvement over that of the first day and practically what ordinarily occurred at the low altitude.

From this series of observations it is evident that the adaptive

changes, which occur within the body during the first days of residence on Pike's Peak, favor the heart during the exertion of walking at the

TABLE I

Effects of three- and four-mile walks

DATE	PLACE	PULSE RATE			ARTERIAL PRESSURES IN MM. HG.					
					Systolic			Diastolic		
		Before	After	Change	Before	After	Change	Before	After	Change
				Three-mile walks						
				(Cheley)						
Average..	Colo. Sp.	69	80	11	113	112	−1	88	88	0
Oct. 15...	Pike's P.	86	120	34	106	134	28	87	91	4
Oct. 16...	Pike's P.	72	102	30	112	128	14	88	89	1
Oct. 17...	Pike's P.	75	108	33	110	122	12	88	88	0
Oct. 18...	Pike's P.	76	102	26	124	132	8	88	88	0
				(Schneider)						
Average..	Colo. Sp.	71	82	11	114	119	5	88	88	0
Oct. 15...	Pike's P.	82	132	50	126	143	17	89	98	9
Oct. 16...	Pike's P.	102	132	30	126			90	94	4
Oct. 17...	Pike's P.	92	120	28	118	126	8	88	90	2
Oct. 18	Pike's P.	90	108	18	121	122	1	87	90	3
				Four-mile walks						
				(Cheley)						
Average..	Colo. Sp.	70	93	23	113	119	6	88	89	1
Oct. 15...	Pike's P.	83	144	61	106	150	44	88	95	7
Oct. 16...	Pike's P.	76	114	38	105	132	27	87	91	4
Oct. 17	Pike's P.	72	126	54	114	132	18	87	91	4
Oct. 18...	Pike's P.	72	126	54	119	142	23	88	92	4
				(Schneider)						
Average..	Colo. Sp.	71	100	29	114	120	6	88	90	2
Oct. 15...	Pike's P.	90	150	60	118	150	32	88	102	14
Oct. 16...	Pike's P.	90	150	60	125	140	15	89	94	5
Oct. 17...	Pike's P.	84	141	57	114	142	28	89	94	5
Oct. 18...	Pike's P.	82	132	50	116	142	26	87	96	7

rate of three miles per hour. The influence of low barometric pressure was manifest these first days by the greater acceleration in the heart

rate, in the great extension in the time required for the rate to return to normal, and in the plateau which occurred in the curve describing the return to the normal rate. This plateau was practically always present. Following this exercise the secondary ascent in the curve noted by Stern (9) was present only twice, once for each subject.

Walks at the rate of four miles per hour for fifteen minutes. As would be expected, the after effects on the heart rate from walking for fifteen minutes at the rate of four miles per hour in Colorado Springs are more marked than when walking for the same length of time at three miles an hour. The amount of acceleration is greater, the return to normal is delayed, and a plateau in the downward curve is the rule rather than the exception. Our data for studies of this form of exercise at the two altitudes appear in part in Table I.

Cheley had in Colorado Springs after this rate of walking an average increase in the pulse rate of 33 per cent and returned to normal in from six to twenty-two minutes. On the first afternoon spent on Pike's Peak this walk sent the pulse from 83 to 144 beats per minute or 73.5 per cent; it slowed quickly to 114 and more slowly to 90 where it continued for five minutes; it then went down to 84 for two minutes and after this returned to 87 where it remained. On the second day with an acceleration of 50 per cent the retardation went through much the same course. Starting with 76 as the normal at 10.40 a.m. it was at 84 an hour and a half after work ceased. On the third day the rate increased from 72 to 126 or 75 per cent, then fell to 78 in twenty-five minutes. On the fourth day exactly the same increase from the same normal was obtained, but the heart rate was still at 81 when the work was interrupted thirty minutes after walking ceased. A plateau appeared each day and in three the secondary ascent noted by Stern also occurred. Cheley's reaction to this amount of exercise did not show marked improvement in the four days spent on the Peak.

Schneider was under observation after this form of exercise in the two expeditions, 1914 and 1915. In 1915 his average acceleration in Colorado Springs was 42 per cent and the return to normal occurred within from six to twenty minutes. In the four days spent on Pike's Peak there was only a little improvement in the way he reacted to this amount of exercise. The pulse rate increased 60 beats the first day and 50 on the last day. After each walk the acceleration was greater than 60 per cent and the return toward normal very tardy, in fact the heart seemed to take a higher tempo for several hours after each period of walking.

In the 1914 expedition Schneider walked this rate of four miles per hour for fifteen minutes on nine different days within a period of two weeks (see Table II). His average acceleration in Colorado Springs was then 31 per cent and the return to normal occurred within from five to twelve minutes. On the first day spent at the higher altitude he had an acceleration of 60 per cent, and the heart did not return to 72, the rate previous to the exertion, but remained at 93. A headache came on with the exercise. On the second day the rate went from 90 to 144, 60 per cent, then dropped to 102 where it remained during a half hour period of observation. On the next day the pulse, starting at 86, accelerated 53 per cent, then retarded to 96 where it remained three minutes after which, apparently without cause, it went to 102 for four minutes and then gradually fell during the remainder of an hour. On the third day the amount of acceleration was less and never thereafter showed as great an increase in beats. On the fifth day even with an acceleration of 54 per cent the heart rate returned to normal within twenty-four minutes. From that day the acceleration was around 40 per cent and the time of return to normal was gradually lessened, thus on the fourteenth day the rate came back to normal in seventeen minutes. Schneider, therefore, showed a marked improvement toward the close of the stay on the Peak but always had a greater reaction than in Colorado Springs.

After the second day on the Peak, Havens was not clearly influenced by the altitude when walking on the level at the rate of four miles an hour. Not once was his percentage of acceleration greater than it occasionally was in Colorado Springs. However the first two days showed some delay in the time required for the pulse to return to normal. In Colorado Springs the normal rate was restored in from six to ten minutes. On the first day at the higher altitude the return was made in twenty minutes; on the second day the rate fell to 78 where it remained instead of decreasing to 72, the normal. Every day thereafter there was a complete return in from seven to fifteen minutes. It should be noted that Havens had trained during the spring months for the two-mile run in track athletics.

Sisco was less affected by the altitude than Schneider, but to a greater degree than Havens, when walking at the rate of four miles an hour. He had when in Colorado Springs accelerations varying between 9 and 45 per cent, with an average of 23 per cent; while the rate came back to normal within from seven to fifteen minutes. On the first day of residence on Pike's Peak his pulse rate had increased 59 per cent

immediately after the walk and required thirty-five minutes to come back to normal. On the next day the increase was less but the return was not completed in the thirty minutes of observation. His average increase, after the first day, for the twelve days was 35 per cent, 12 per cent higher than in Colorado Springs. The time required for return to normal was variable, on some days it required twelve and on others as much as twenty-five minutes. Sisco made in the two weeks, therefore, a good return toward his low altitude reaction but even at the last there continued some altitude influence during this exercise.

Atwater and Gregg also served as subjects for the four-mile per hour walk during the four days following their climb to the summit of the Peak. In Colorado Springs each reacted less to this form of exercise than other subjects studied. Atwater's maximum acceleration in Colorado Springs was 13 per cent, with a return to normal within one or two minutes; while Gregg's maximum increase was 17 per cent, followed by a subnormal period with normal restored within five minutes. On the second day spent on Pike's Peak Atwater's pulse rose from 84 to 120 or 43 per cent, returning to 90 in three minutes and remaining there during an observation period of forty minutes. On the next day, when his heart was more irritable, the rate went from 90 to 150 beats per minute or 67 per cent, then quickly fell in two minutes to 84, which was subnormal, where it remained for five minutes and was back to normal eleven minutes after work ceased. On the fourth day the acceleration was 33 per cent and the return was made in nine minutes. In the five days he did not nearly recover his low altitude reaction but showed a marked improvement. Gregg, who was apparently the more affected by the climb, had on the second day an acceleration from 102 to 156 or 53 per cent. His heart rate failed to return to normal in eighteen minutes, but came down to 108 and remained there for several hours. There was some improvement during the next three days, in that the return to normal occurred within from seven to twenty-five minutes; but he did not, however, react as in Colorado Springs.

The influence of the fatigue due to the climb was not as marked on Atwater and Gregg during the walk at four miles per hour as was to be expected in view of the observations on the early morning rate and the daily mean pulse rate for the sitting posture. Nevertheless considering that both men were less influenced by this walk in Colorado Springs than our other subjects we are inclined to believe that the fatigue did make their hearts more irritable than altitude alone would

have done. Physical fitness no doubt accounts in part for the differences in reaction seen among our subjects, but the factors are difficult to analyze.

The data gathered from our study of walks show clearly that at high altitudes, during the first days of residence, there is a greater heart reaction to a given exercise than after adaptive changes have set in. At first the amount of acceleration and the time required for return to normal rate are as a rule markedly increased. Each man studied showed a return toward the low altitude reaction, in Havens this was complete in two days, in others it was not complete at the end of two weeks residence at the higher altitude. The number of heart beats per minute, both before and after exercise, was for all subjects clearly above the low altitude rate. Following the four-mile per hour walks on Pike's Peak the plateau practically always appeared, but the secondary ascent only occasionally.

A more rapid walk. An experiment was made on Cheley at both altitudes after a more rapid walk. In Colorado Springs he walked for fifteen minutes at the rate of five and one-half miles per hour. In consequence his pulse rate rose from 63 to 158 and returned to normal in twenty minutes. On the second day at the higher altitude he walked for ten minutes at five miles an hour, with the result that his pulse rate accelerated from 78 to 180. It then fell in four minutes to 108 and more gradually in the next thirty minutes to 100, where it remained for over an hour when observations were discontinued. Cheley felt very uncomfortable for some time after this walk and was not willing to repeat it later, while in Colorado Springs he was only breathless after the greater exertion.

The after effects of a short rapid run. A run of 175 yards up the "Cog" road track in from thirty to forty-five seconds gave a maximum of effort. One half of this distance was on the level, the remaining distance had in part approximately a 25 per cent grade. In order to do, in Colorado Springs, a comparable amount of work in an equal period of time it was necessary to run 260 yards through the corridors of one of the college buildings, including the ascent of two flights of stairs. As a result of the run in Colorado Springs the acceleration of the heart was between 38 and 90 beats per minute or to from 40 to 176 per cent, and the rate frequently returned to normal within fifteen minutes and never required as much as an hour.

It was difficult and exhausting to make the run on Pike's Peak. On the first day, although the runner went as fast as possible, the best

time made was between 40 and 45 seconds. Furthermore each man felt like quitting before reaching the end. After several days had been spent on the Peak the effort was not so great and the distance could be covered within from 30 to 35 seconds. The time required for the rate to return to normal was so long that we found it necessary to leave this form of exercise until late afternoon when other experiments had been finished. After these runs the heart of each subject took and held for several hours a rate ten to twenty beats above normal. The data for these runs appear in Table III.

Havens made the run on Pike's Peak ten times, the heart rate increased to from 72 to 206 beats per minute, with an average of 121; the percentage acceleration varied between 86 and 219. For Schneider in six runs the rate increased between 72 and 162 beats, average 105, and the percentage change ranged between 75 and 208 per cent. Sisco ran seven times, the heart rate increased to from 108 to 174 beats per minute, with an average of 135 beats; his percentage increase varied from 125 to 223. Atwater ran once and had an increase of 204 beats or 283 per cent.

Lowsley (11) studied the increase in the heart rate after exertion for five forms of exercise, moderate, rapid, vigorous, fatiguing, and exhausting. They have been named in order of an ascending scale as to heart acceleration. The average increase was after moderate 26, after rapid 33.5, and after exhaustive exercises 54 beats per minute. The greatest acceleration noted by him was 80 beats per minute. He found that the heart rate returned to normal within about one-half an hour after moderate exercise and one hour after rapid exercise; while it required three and a half hours after exhaustive exertion. Our runs in Colorado Springs give about the same effects that Lowsley obtained after rapid exercises; while those on Pike's Peak accelerated the heart rate far more than the most exhaustive exercise studied by him and the slowness with which the heart rate returned to normal corresponded with that of his exhaustive exercises. The exhaustive exercises studied by Lowsley were ten and twenty-mile races. It is evident, therefore, that the heart is put to a very severe test at high altitudes by rapid vigorous exercise.

B. Changes in pulse rate during the period of work

We used a stationary bicycle for this series of observations. The devise was somewhat unsatisfactory in that we could not with exactness control the amount of resistance to be overcome. Our data do

not, therefore, permit of exact comparisons from the standpoint of work done. In each experiment the subject drove the bicycle at the same rate for from fifteen to twenty minutes. The pulse rate was counted for ten second intervals. The data obtained in Colorado Springs in nearly every instance correspond with those of Bowen (10) and of Lowsley(11). There occurred at first a rapid primary rise in pulse rate when work began, lasting from one to four minutes, and then, either without a pause or following a plateau, a gradual secondary rise which apparently in some of the experiments would have gone higher had the work been longer continued. Most of our data for this work on the bicycle were obtained on Havens, Schneider, and Sisco. A single experiment at both altitudes was performed on Eager and Munro.

The observations on Pike's Peak, in the 1914 expedition, were made on the third, eighth, and eleventh days. The response of the heart at the high altitude was very different from that found to occur at the low altitude. In five of the nine experiments the maximum rate was reached within a half minute after work began. In the other four the maximum came in the primary rise within from one to five minutes. The maximum was always followed by a marked retardation which finally ended in a plateau. Occasionally a secondary rise followed toward the end of the work period but the rate rarely again approached the maximum of the primary rise. Havens and Sisco always reached their maxima within the first minute of work, Schneider's pulse rate increased more gradually and once reached the maximum as late as five minutes after work began. In the last experiment on Schneider the primary maximum was reached in one minute, four minutes later the slowest rate occurred and this was followed by a gradual secondary rise which, toward the end of the work period, carried the rate back to the maximum of the primary rise.

The experiments on Pike's Peak with Eager and Munro, who walked up, show the same general curve of acceleration. The primary rise in each lasted four minutes, after this there was some retardation. Eager's pulse rate went from 96 to 130 in four minutes, and then retarded for four minutes to 120, after which it varied between 120 and 124. Munro's heart accelerated in four minutes from 96 to 138, and later retarded and varied between 130 and 134.

ARTERIAL PRESSURES

In an earlier paper (1) we presented data on the arterial pressures obtained from men leading a comparatively inactive life. In the majority of men studied the high altitude did not influence the arterial pressures, yet in some it caused a slight fall, and in one man a marked rise.

In our later expeditions the daily routine demanded greater activity, each day the members of the party took part in several physical exercise experiments. It may be worth while, therefore, to compare control records taken at both altitudes just before the beginning of the physical work of the experiment. In every case the control determinations were made only after the subject had been sitting quietly for at least five minutes and had not been exercising within an hour, although he was permitted during this time to be busy with laboratory duties.

Atwater, Cheley, Gregg, and Havens had practically the same averages at both altitudes, as well as corresponding variations. During the first two days of each expedition to the high altitude Schneider had higher pressures than at the low altitude. After this period of high pressure his average was a few millimetres less than in Colorado Springs. He showed a disposition during the 1914 expedition, when the amount of exertion taken daily was greatest, to have a rise in the systolic pressure of from 4 to 6 mm. Hg during the latter part of the afternoon. This was only noticeable on the days in which the program of experiments was crowded.

Sisco was a member of three expeditions to Pike's Peak, in the spring and autumn of 1913, and in June 1914. Prior to the first two his Colorado Springs averages were: systolic 118 and 119 mm., diastolic 85 and 86 mm., pulse pressure 33 mm. During the corresponding sojourns on Pike's Peak the following averages were obtained: systolic 117 and 115 mm., diastolic 84 and 85 mm., pulse pressure 33 and 30 mm. Hg. While there was no change in the first there was a fall in the pressures in the second expedition. Prior to the 1914 expedition all of Sisco's pressures averaged higher than ever before, the systolic was 125, diastolic 89, and pulse pressure 36 mm. During the first two days spent on Pike's Peak his pressures averaged about the same, but thereafter throughout the remainder of the two weeks stay each was decidedly higher. The averages were: systolic 130, diastolic 95, and pulse 35 mm. Hg. Furthermore Sisco showed the same late afternoon rise that was noticed in Schneider. We were unable to account for the high

pressures in Sisco. That altitude was the sole cause of the rise seems improbable because of the fact that his arterial pressures were, even before the ascent, above what we had ordinarily found in Colorado Springs.

All arterial pressure determinations for the expeditions prior to 1915 were made with an Erlanger sphygmomanometer and those in 1915 with a Tycos sphygmomanometer.

A. The changes in arterial pressure after exercise.

Ordinarily at the close of a work period the arterial pressure is up but it at once begins to decrease. Bowen (10) finds that the fall in the pressure is not so rapid as the primary fall of the pulse rate which it accompanies and that a subnormal period follows. Lowsley (11) studied the systolic, diastolic, and pulse pressures after work and finds that these invariably fall below normal and remain in this subnormal condition for a considerable period. The systolic falls more rapidly than the diastolic pressure.

The after effects of walking at three miles per hour for fifteen minutes. Cheley reacted to this walk in Colorado Springs with a slight fall of from 1 to 3 per cent in the systolic pressure, while the diastolic pressure remained unchanged. In several instances the return to normal was observed and was found to occur within from three to seven minutes. During the four days spent on Pike's Peak he had after the walk a marked rise in the arterial pressures but progressively decreased the amount of reaction with each day of residence. During the first afternoon the systolic pressure rose 26.4 per cent and remained up thirty minutes, the diastolic went up 4.6 per cent and returned to normal within three minutes. On the second day the systolic increased only 14.3 per cent and returned to normal, without going through a subnormal period, in ten minutes; while the diastolic pressure only went up 1.1 per cent and returned in two minutes. On the third day the systolic pressure increased 10.9 per cent. The return, which was less rapid than on the second day, required eighteen minutes. On the fourth day, as on the third, the systolic alone increased and this time only 6.4 per cent, it then quickly went to subnormal. The pulse pressure following these walks in Colorado Springs was as a rule lowered, while on the Peak it went up to from 8 to 24 mm. While Cheley showed a marked improvement at the higher altitude nevertheless the reaction was, even on the last day, decidedly above any obtained with the same exercise in Colorado Springs.

The experiments upon Schneider while on the Peak gave irregularities. In Colorado Springs this walk raised his systolic pressure from 1 to 7 per cent and the diastolic either not at all or not more then 1 per cent. The return to normal was rapid, and occasionally there occurred a subnormal period of short duration. Following the walk on the first afternoon spent on Pike's Peak, in October 1915, his systolic pressure was up 13.4 per cent and the diastolic 10.1 per cent. Afterward the systolic went subnormal but was back to normal within ten minutes, while the diastolic returned to normal in six minutes. On the following days the systolic pressure did not clearly rise more than it frequently did in Colorado Springs, but the diastolic rose from to 2.3 to 4.4 per cent.

Arterial pressure changes after walking at four miles per hour for fifteen minutes. In October 1915 both the systolic and diastolic pressures were determined, while in 1914 only the systolic pressure was recorded. Since the 1915 data cover both they will be discussed first. See Table I.

When in Colorado Springs this walk raised Cheley's systolic pressure as much as 3.5 to 7 per cent and the diastolic pressure 0 to 2.3 per cent. After work ceased the fall in pressure always carried the systolic pressure into a subnormal period for from 3 to 10 minutes, after which it returned to normal. During the first day spent on Pike's Peak the walk raised the systolic pressure 41.5 per cent and the diastolic 8 per cent, both returned to normal within fifteen minutes but did not become subnormal. On the second day the increase was somewhat less, systolic 25.7 per cent, and diastolic 4.6 per cent. The diastolic returned to normal in four minutes, the systolic pressure was still above normal twenty-five minutes after work ceased. On the third day the systolic rose only 15.8 per cent and returned to normal within ten minutes. While on the fourth or last day it rose 19.3 per cent, was subnormal fifteen minutes later and was not back in twenty-five minutes. A diastolic increase of 4.5 per cent occurred the last three days. With this as after the slower walk Cheley had the greatest reaction on the first day and considerably less on the following days. It will also be observed that with greater exertion the altitude influence became more pronounced.

The after effects of the four-mile per hour walk on Schneider's arterial pressures have been studied during two expeditions. In Colorado Springs this work raised his systolic pressure from 4 to 9 per cent, with an average increase of 6 per cent and the diastolic from 0 to 3

per cent or an average of 2 per cent. Each pressure returned to normal within about five minutes, and practically always passed through a brief subnormal period. In 1915, when both the systolic and diastolic pressures were determined, Schneider reacted during the first afternoon spent on the Peak with a rise in systolic pressure of 27 per cent, and in diastolic of 15.9 per cent. Both pressures returned to normal within fifteen minutes. On the second day a systolic increase of only 12 per cent was obtained, but the normal, or control pressure, 125 mm. was abnormally high. After the walk ceased the pressure quickly went subnormal to 114 and did not return in thirty-five minutes. On the two following days both pressures rose a greater number of millimetres and each time the subnormal was more prolonged than in Colorado Springs. In the 1914 expedition when only the systolic pressure was determined Schneider also showed throughout the stay of two weeks a greater rise than in Colorado Springs. These data will be found in Table II. On the first day of this sojourn the systolic pressure rose from the high level of 128 mm. to 148 mm. of Hg or 16 per cent, the return to normal was slow and without a subnormal stage. The high pressure found before exercise was associated with oncoming mountain sickness. On the second day the reaction was 20 per cent. Thereafter the rise in systolic pressure was not so great; but it was, with one exception, always greater than followed the same exertion at the low altitude.

The pulse pressure changes after the walk of four miles an hour were greater on Pike's Peak for both Cheley and Schneider. Cheley's pulse pressure increased in Colorado Springs only from 2 to 8 mm. Hg. The first day on the Peak the walk raised it 37, the second day 23, the third day 14, and the fourth 19 mm. Schneider's increase in Colorado Springs was from 5 to 7 mm. For the four days spent on the Peak the rise was 18, 10, 23, and 17 mm. Hg respectively.

Systolic pressure determinations made on Havens and Sisco after the four-mile per hour walk show, on the whole, similar changes and also bring out the fact that all men do not react to the same degree when under the influence of lowered barometric pressure. Havens systolic rise in Colorado Springs varied from 0 to 7 per cent, with an average of 2 per cent, the return was accomplished quickly and rarely passed into a subnormal period. On Pike's Peak his increase ranged between 6 and 11 per cent. It was not more the first day than after long residence but his pressure invariably went subnormal for a time. During the first four days the return to normal required from 7 to

TABLE II

Walks at four miles an hour

DATE	PLACE	PULSE RATE			SYSTOLIC PRESSURE IN MM. Hg			VENOUS PRESSURE IN CM. H_2O		
		Before	After	Change	Before	After	Change	Before	After	Change
				(Havens)						
Average..	Colo. Sp.	70	94	24	127	130	3	12.4	14.8	2.4
June 16...	Pike's P.	69	81	12	122	132	10	1.5	6.0	4.5
June 17...	Pike's P.	72	90	18	126	140	14	7.5	11.5	4.0
June 18...	Pike's P.	81	102	21	126	138	12	10.0	14.7	4.7
June 19...	Pike's P.	84	120	36	122	130	8	12.8	18.3	5.5
June 20...	Pike's P.	74	102	28	132	140	8			
June 22...	Pike's P.	84	120	36	132	146	14	10.6	12.6	2.0
June 24...	Pike's P.	88	102	14				7.9	11.0	3.1
June 26...	Pike's P.	90	108	18	121	134	13			
June 29...	Pike's P.	70	96	26	130	138	8			
				(Schneider)						
Average..	Colo. Sp.	80	105	25	117	122	5	16	17.1	1.1
June 16...	Pike's P.	75	120	45	128	148	20	18.6	25.3	6.7
June 17...	Pike's P.	90	144	54	122	146	24	11.4	14.1	2.7
June 18...	Pike's P.	86	132	46	118	134	16	20.7	17.4	−3.3
June 19...	Pike's P.	91	132	41	119	134	15	11.9	13.8	1.9
June 20...	Pike's P.	84	129	45	120	138	18	11.8	12.9	1.1
June 22...	Pike's P.	87	132	45						
June 23...	Pike's P.	90	126	36	118	124	5	15.1	16.1	1.1
June 26...	Pike's P.	90	126	36	118	136	18			
June 29...	Pike's P.	92	132	40						
				(Sisco)						
Average..	Colo. Sp.	71	87	16	128	133	5	10.1	11.0	0.9
June 16...	Pike's P.	87	138	51	122	138	16	14.2	14.5	0.3
June 17...	Pike's P.	75	102	27	122	134	12	6.0	15.1	9.1
June 18...	Pike's P.	96	120	24	130	143	13	−0.5	11.0	11.5
June 19...	Pike's P.	87	114	27	130	144	14	1.6	2.2	0.6
June 20...	Pike's P.	75	114	39	128	135	7	6.4	8.8	2.6
June 24...	Pike's P.	93	132	39	132	144	12	7.2	8.3	1.1
June 26...	Pike's P.	90	114	24	134	143	9	0.0	3.9	3.9
June 28...	Pike's P.	78	102	24	128	140	12	2.8	12.1	9.3

12 minutes, which was longer than in Colorado Springs. After these first days it returned to normal in from three to seven minutes, which was still slightly above the average time required in Colorado Springs.

Again it should be noted that Havens was in excellent physical condition as a result of athletic training.

Sisco gave in Colorado Springs after the four-mile per hour walk an increase of from 3 to 9 per cent in the systolic pressure. During the first day on Pike's Peak the rise was 13 per cent and on the next three days was 10 per cent. Several times thereafter the rise was about the same as occurred at the lower altitude. Sisco's normal, however, was during this period almost continuously from 4 to 6 mm. above his Colorado Springs average. It is evident then that on the Peak after this walk his systolic pressure was uniformly higher than after the same exercise in Colorado Springs. For the first two days the return to normal was delayed from 50 to 100 per cent.

In order to determine whether the fatigue due to climbing the Peak would accentuate the altitude arterial pressure reaction we had Atwater and Gregg take the four-mile per hour walk on the four days following the ascent. Atwater's systolic pressure rose 20, 25, 20, and 8 per cent; Gregg's went up 15, 22, 34, and 9 per cent. The time required for the pressure to return to the normal was greatly prolonged in the first experiment and shorter thereafter. The reaction of these two men was not as great as was obtained by Cheley and Schneider but greater than for Havens and Sisco. The experiments on the last day, when the pressures rose only 8 and 9 per cent respectively, indicate that these men reacted well to the altitude influence. A similar improvement was noted in the reduced amount of acceleration in the heart rate. It is quite evident, therefore, that the fatigue of the climb did not materially alter the high altitude arterial pressure reaction for this amount of physical work.

Our arterial pressure studies following the walks show that the pressures are higher, after a given rate of walking, on the Peak than after the same amount of work at a lower altitude. On comparing the changes resulting from walking at the two rates, three and four miles an hour, we find that the greater the exertion the more pronounced is the influence of lowered barometric pressure. It is also evident that the altitude influence is most marked during the first days of residence on the Peak.

The after effects of a short rapid run on systolic pressure. Rapid runs of 260 yards with the ascent of several flights of stairs in Colorado Springs caused the systolic pressure to increase between 25 and 67 mm. Hg. The average rise was 31 mm., while the percentage of increase varied between 17 and 58. The pressure invariably went

subnormal within from 9 to 15 minutes, and was normal again within twenty minutes. Lowsley found, after the 100-yard dash, that the average rise in the systolic pressure of nineteen men was 36 mm. A subnormal depression of from 15 to 25 mm. followed while the return to normal required as much as one hour and ten minutes. The data obtained on Pike's Peak appear in Table III.

Havens' reacted to the 175-yard run when on Pike's Peak with a rise in systolic pressure that ranged from 56 to 72 mm. Hg, an average of 67 mm. The percentage rise varied between 40 and 64. The later changes were followed for from 20 to 50 minutes and in no instance was the normal restored. His return to normal and into the subnormal period was very irregular. On the first day the pressure went up from 106 to 174 mm. and in 38 minutes had only fallen to 126. The next day it went into the subnormal phase within ten minutes. The fall into the subnormal phase varied between 9 and 36 minutes. Havens showed no definite improvement in reaction during a residence of two weeks.

Schneider's systolic pressure, as the result of the run in Colorado Springs, rose from 25 to 30 mm., while on the Peak the rise varied from 37 to 65, with an average of 52 mm. In Colorado Springs the depression into the subnormal period occurred within from 9 to 13 minutes. Following the first three runs on the Peak the pressure remained above the normal during the periods of observation which were 35, 28, and 30 minutes respectively. For every run thereafter his pressure went into the subnormal period within from 11 to 15 minutes. This reduction in the period of high pressure was Schneider's only improvement in the two weeks.

Sisco showed the same marked increase in the systolic pressure at the high altitude that was obtained on Havens and Schneider. This increase varied between 47 and 82, with an average of 63 mm. Only once did he go into the subnormal period during the time of observation and then this required twenty minutes. His pressure after work remained above normal as long as from twenty to thirty-five or more minutes. No improvement was noted during the two weeks.

The rise in blood pressure found after these short quick runs on Pike's Peak is in general comparable to the increase in systolic pressure obtained in exercises of maximum muscular effort. McCurdy recorded the systolic pressure in Boston for twenty-three men during an exercise of the maximum lift for each man, the weight lifted varied from 118 to 249 kilos. The average rise in systolic pressure was 69 mm. The

TABLE III

Short runs on Pike's Peak

DATE	PULSE RATE			SYSTOLIC PRESSURE IN MM. Hg		
	Before	After	Increase	Before	After	Increase
(Havens)						
June 16	78	162	84	106	176	70
June 17	84	156	72	144	210	66
June 18	78	168	90	134	200	66
June 19	81	180	99	126	198	72
June 20	90	258	168	138	202	64
June 21	90	252	162	134	200	66
June 22	94	300	206	140	196	56
June 23	90	240	150			
June 25	90	180	90	122	194	72
June 28	81	168	87	123	194	71
Average	85	206	121	130	197	67
(Schneider)						
June 17	96	168	72	120	158	38
June 18	78	240	162	127	176	49
June 19	88	180	92	124	186	62
June 21	96	216	120	124	186	62
June 25	87	180	93	127	192	65
June 28	90	180	90	127	164	37
Average	89	194	105	125	177	52
(Sisco)						
June 16	72	192	120	122	182	60
June 17	84	192	108	122	170	48
June 18	90	240	150	138	185	47
June 19	78	252	174	144	226	82
June 20	96	216	120	128	204	76
June 21	100	252	152	140	200	60
June 25	68	192	124	128	200	72
Average	84	219	135	132	195	63

lowest increase was 49 and the highest, except for one very unusual case was 108 mm. Hg. As a result of our runs Havens' average increase was 67 mm., only two below McCurdy's average; while Sisco's was 63

and Schneider's 52 mm. Our lowest rise was 37 and the highest 82 mm. McCurdy had seven tests in which the pressure was 200 mm. or above; while Havens and Sisco each on four occasions had pressure of 200 mm. or more. It appears then that the heart and blood vessels, in these exercises were subjected to almost as great strain as occurs in the most severe test the heart must ever undergo.

Robison, who was acclimatized to the altitude of 14,109 ft. by a residence of five and one-half months, made this run with the result that his pressure rose from 104 to 158 mm., a rise of 54 mm. This exceeds the average in Colorado Springs and suggests that long residence at the high altitude does not much reduce this increase.

B. The changes in the arterial pressure accompanying exertion

The changes in arterial pressure during exercise have been considered at low altitudes by Bowen (10) and Lowsley (11). These found a rise in pressure when work began which reached a maximum in from five to twenty-five minutes. This followed after the primary rise in pulse rate. While the primary rise in pulse rate occurred in from one to three minutes, the pressure rise required four or more minutes. The diastolic pressure rose and either followed the systolic curve or occurred somewhat later.

We have studied the blood pressure changes during two forms of work. The systolic was determined for five subjects while riding for from fifteen to twenty minutes on the stationary bicycle, and the systolic and diastolic on two subjects for a period of six minutes during which they, while in the reclining position, alternately raised and lowered the legs. In each kind of work the rate of movement was the same at the two altitudes.

The study during work on the bicycle was of the systolic pressure alone. Experiments during the 1914 expedition were made on the third, eighth, and eleventh days. In Colorado Springs we obtained during the work period, curves similar to those reported by Bowen and by Lowsley.

Havens' systolic pressure rose to the maximum in practically the same time at both altitudes. In three typical experiments in Colorado Springs the pressure rose gradually to the maximum in 10, 11, and 12 minutes respectively. The maximum was reached on Pike's Peak in the first experiment in 11, in the second in 13, and in the third in 6 minutes. The rate of rise was more rapid during the earlier minutes

of exercise on the Peak. His systolic pressure rose in three minutes in Colorado Springs 14, 16, and 20 mm.; and on Pike's Peak in the same time 22, 24, and 24 mm. respectively. Schneider's systolic pressure also rose more rapidly on the Peak than at the lower altitude. In Colorado Springs the maximum was reached in from 12 to 15 minutes. On Pike's Peak it rose to the maximum in five minutes during the first, in nine minutes in the second, and in three minutes in the third experiment. Sisco also reacted more quickly at the high altitude. His rise in Colorado Springs was made in from twelve to fifteen minutes. The first experiment on the Peak gave the maximum in eight, the second in four, and the third in three minutes.

Since the effort during work could not be exactly controlled a comparison of the total amount of rise in the systolic pressure obtained at the two altitudes will not give as reliable evidence on the influence of altitude as the data for the walks and for leg raising. Haven's rise in Colorado Springs varied between 22 and 34 mm., on the Peak between 26 and 30 mm. Schneider had, in each experiment in Colorado Springs, a rise of 23; on the Peak from 20 to 34 mm. Sisco's rise in Colorado Springs was around 18 mm. and on the Peak varied between 22 and 35 mm. Schneider and Sisco reacted with a slightly greater rise at the higher altitude, Havens with the same at both.

Single bicycle experiments at both altitudes on Eager and Munro show their rise in pressure during exercise at the high altitude to be more rapid. Eager's systolic pressure rose in the first four minutes 4 mm. in Colorado Springs and 10 mm. on the Peak. Munro's pressure rose 6 mm. in two minutes in Colorado Springs, and 16 mm. on the Peak.

The leg raising exercises were conducted on Cheley and Schneider in the 1915 expedition. Two experiments were made on each subject while on Pike's Peak. While the exercise was not continued long enough to obtain the maximum rise yet in each experiment both the systolic and diastolic pressures rose more rapidly than in Colorado Springs. In the two studies on Cheley when on the Peak the systolic pressure rose 24 and 11 mm. Hg in three minutes, in Colorado Springs in the same time it rose 7 and 8 mm. For Schneider the increase in three minutes on the Peak was 28 and 34 mm. Hg and in Colorado Springs from 22 to 24 mm. respectively. The total rise in systolic pressure on Pike's Peak for Cheley was 27 and 14 per cent in the two experiments and for two in Colorado Springs it was 8 and 10 per cent. Schneider's rise in systolic pressure in Colorado Springs ranged between 25 and 30 per

cent; on the Peak the first experiment gave an increase of 33 per cent, and the second 39 per cent.

The diastolic which was determined during the leg raising exercise followed the systolic pressure. The total rise was greater on the Peak. For Cheley the diastolic increase in Colorado Springs was 1 and 2 per cent; in the first exercise on the Peak it was 4 per cent, and in the second 6 per cent. The diastolic rise obtained on Schneider in Colorado Springs varied between 0 and 2 per cent, on the Peak it was 9 and 8 per cent respectively. Both subjects had a greater pulse pressure during exercise on Pike's Peak but Cheley had a greater increase than Schneider.

The studies of the arterial pressure changes during exercise show clearly that there occurs a more rapid rise in the pressure at the high than at the low altitude. The rate of rise is not so rapid as that of the pulse rate, the pressure rise lagging somewhat behind the acceleration in pulse rate. The total amount of rise in the arterial pressure also is, in general, greater during work on Pike's Peak than in Colorado Springs. One of our subjects, Havens, did not have a greater increase in pressure at the high altitude, but as noted before he was in better physical condition because of participation in athletics than others studied. The greater rise noted during exertion accords with our data obtained from the study of the after effects of work.

The influence of low barometric pressure during and immediately after exertion reveals itself in a more marked rise in all the arterial pressures, and in the prolonged delay in return to normal. The effects are more pronounced during the first days of residence at the high altitude. The improvement resulting from the changes of acclimatization is only evident for very moderate exertion. The greater the exertion the more pronounced will be the altitude effects upon the rise in pressure and the delay in return to normal.

VENOUS PRESSURE

In our earlier report (1) it was stated that in five out of six men studied the venous pressure was as much as 25 to 87 per cent lower on Pike's Peak than in Colorado Springs. Havens and Sisco showed the fall in venous pressure in three trips to the Peak, while Schneider was not affected in four trips. Three additional men have now been examined and found to have a lessened venous pressure at the high altitude. The fall in pressure was for Atwater 40 per cent, Cheley 25 per cent, and Gregg 60 per cent.

The effect of exercise upon the venous blood pressure

The changes in venous pressure while riding a stationary bicycle. That the venous pressure rises during exercise can be demonstrated by a casual observation of the superficial veins of the hands during exertion. Hooker (13) investigated the extent of this rise at a low altitude and noted the time required to reach the maximum pressure in men working on a stationary bicycle. In nine experiments the venous pressure in the superficial veins of the hand rose between 6 and 14 cm. of water, and reached the maximum in from two to forty-two minutes, in six out of nine tests this was reached in less than fifteen minutes.

Our own experiments made on five subjects while riding on the stationary bicycle were continued for fifteen and twenty minutes. As has been stated earlier we were unable to regulate with exactness the amount of work done on the bicycle, nevertheless the work done, which was approximately the same, produced marked differences in results at the high altitude. During this work in Colorado Springs, Havens gave a rise in venous pressure in four experiments of from 1.6 to 6 cm. of water; on Pike's Peak, also in four experiments, the rise ranged between 3.2 and 11 cm. The minimum and maximum were both somewhat higher on the Peak. Schneider's venous pressure during rest is scarcely affected on the Peak. During this form of exercise in Colorado Springs his venous pressure rose to from 4.9 to 6 cm. and on Pike's Peak in three experiments from 1.7 to 4.9 cm. He, therefore, reacted less rather than more. Sisco, whose venous pressure during inaction is uniformly low at the high altitude, had increases in venous pressure in Colorado Springs while working on the bicycle of from 4.4 to 7.4 cm.; while in three experiments on the Peak the rise was 8.4, 9.1, and 9.4 cm. respectively.

A single experiment on each Eager and Munro was made two days after they had walked up the mountain. Each man had a greater rise in pressure on the Peak than in Colorado Springs. Eager's rose in Colorado Springs from 13.1 to 16.7 cm. or 3.6 cm. in twenty minutes, and on the Peak from 3.6 to 11.8 cm. or 8.2 cm. In Colorado Springs Munro's venous pressure rose from 16.1 to 20.7 or 4.6 cm., while on the Peak it went up from 2.6 to 15.8 or 13.2 cm. of water in twenty minutes.

In four out of five subjects work on the bicycle caused, on the average, a greater increase in the venous blood pressure at the high altitude. The maximum pressure during work was not as high on Pike's Peak in any one of these subjects as in Colorado Springs. This is

accounted for by the fact that each had in rest a lower venous pressure while on the Peak. We were unable to find any regular differences in the time taken to reach the maximum venous pressure during the period of work at the two altitudes.

The after effects of exertion on the venous blood pressure. The changes in venous pressure were studied on five men after walking for fifteen minutes at the rate of four miles an hour. In Colorado Springs the pressure almost invariably went subnormal for a period within from eight to twelve minutes after work ceased, but on Pike's Peak a subnormal period was observed only twice and both of these occurred in Havens. The time required to reestablish the normal pressure was not appreciably different at the two altitudes.

The rise in venous blood pressure noted immediately at the end of the walk merits a more detailed statement. These data appear in Table II. As a result of these walks in Colorado Springs Havens' venous pressure rose from 1.5 to 3.8 cm. During the first four days of residence on the Peak the following rises were observed 4.5, 4.0, 4.7, and 5.5 cm. of water. On the seventh and ninth days the rise was less, 2 and 3.1 cm. respectively. Schneider reacted in Colorado Springs, for this amount of work, with increases in venous pressure of from 0 to 5.3 cm. On the first afternoon on the Peak, in the early period of mountain sickness, this walk increased the pressure 6.7 cm. During the remainder of the stay the rise in pressure was not greater than occurred in Colorado Springs. Thus five experiments in a period of nine days gave the following increases: 2.7, 1.9, 1.1, and 1.0 cm. and one reaction in which there was a decrease in pressure of 3.3. cm. of water. Sisco's venous pressure rose only slightly as a result of this walk in Colorado Springs—0.3 to 1.7 cm. There was practically no reaction on the first afternoon on the Peak. During the following ten days six experiments on him gave respectively 9.1, 11.5, 0.6, 2.4 1.1, 3.9, and 9.3 cm. of water rises in venous pressure.

The venous pressure reaction after these walks was carefully studied on Atwater and Gregg after they had climbed the Peak but was neglected in Colorado Springs. If, however, it is kept in mind that the venous pressure seldomly increases more than 5 or 6 cm. in young men in Colorado Springs as the result of walking for fifteen minutes at four miles per hour the data obtained from them on the Peak is of interest. Both men made the walk four times while on the summit, the first on the second day of residence. Gregg reacted with the following rises: 4.4, 9.2, 10.2, and 7.2 cm.; all except the first were greater

than would have occurred in Colorado Springs. Atwater reacted differently. As a result of the first walk on the second day his venous pressure fell 2.1 cm., on the third day 10.8 cm., on the fourth day 1.8 cm.; while on the fifth and last day for the first time it rose 1.4 cm. On the last day his pulse rate and arterial pressure also reacted more nearly as at the lower altitude.

The study of the after effects of this walk on the venous pressure has shown the same general reaction that occurred during the work on the stationary bicycle. Schneider's venous pressure in this form of exercise, with the exception of the first day, was not influenced by low barometric pressure. Gregg, Havens, and Sisco clearly reacted with a greater rise in pressure; while Atwater on the first days reacted with a fall in pressure during the exertion.

PULSE RATE AND BLOOD PRESSURE CHANGES AFTER WALKING UP PIKE'S PEAK

The heart beat, the arterial and venous blood pressures were determined on Atwater and Gregg at intervals during a period of seven hours after they arrived on the summit. Both on arrival felt well and cheerful after walking a distance of 9.4 miles with a rise of approximately 7700 feet in four hours and fifteen minutes.

The first determinations were made as quickly as possible after they arrived at 12.44 p.m. Our data appear in Table IV. In Colorado Springs Atwater had a systolic pressure of 140, diastolic pressure 90, and pulse pressure 50 mm. His venous pressure averaged 9 cm. of water, and his pulse rate under 70 beats per minute. Two minutes after arriving his pressures were: systolic 146, diastolic 94, and pulse pressure 52 mm. Hg, venous pressure 11 cm. of water, and pulse rate 114. Thus each pressure was only slightly above normal. Practically no change in the pressures occurred within the following twenty minutes, but the pulse rate had retarded from 114 to 102. From that time on the pressures declined, the arterial pressures did not fall equally, the diastolic lagging behind. As a result the pulse pressure fell most rapidly, to 34 within the first hour. An hour and a half later, or about two hours and fifteen minutes after he reached the summit, the pulse pressure had again returned to normal. The systolic and diastolic pressures both reached their minimum values at the same time, two and a quarter hours after the climb ceased. Both of these pressures were, generally speaking, back to normal two hours later. The entire time for the fall in these and the return to normal required for the

systolic and diastolic pressures four hours and fifteen minutes and for pulse pressure two hours and fifteen minutes. These figures correspond with those obtained by Lowsley (11) in his study of exhaustive exercises in which the men at low altitudes ran races of ten to twenty miles. The average times required for his subjects to return to normal were for systolic slightly less than four hours (232 minutes), diastolic two and two-thirds hours (160 minutes), and pulse pressure two and a half hours (152 minutes). In his studies of moderate, rapid, vigorous, and fatiguing forms of exercise the time for return to normal for systolic pressure rarely approached two hours, for diastolic one hour, and for pulse pressure one and one-half hours. The time required by Atwater to return to normal clearly shows the exhaustive nature of the climb to the summit of Pike's Peak. The total fall in the pressures was not as great as often follows many forms of exertion. A fall in systolic arterial pressure was noted by Durig and Kolmer (3) in all four of their subjects shortly after the climb to the summit of Monte Rosa. Explanations offered were that in one subject it was due to heart fatigue and in two to skin irritation. Undoubtedly each man was in the subnormal phase, which invariably follows exertion, at the time the determination was made. They made only a single observation on each man. Atwater's venous pressure began to fall at once on arrival. This resulted in a negative pressure of 4.2 cm. of water at the end of three hours. His venous pressure was still negative the following morning but within the twenty-four hours again became positive.

The pulse rate gradually retarded until, four hours and fifteen minutes after the ascent, it had reached 84 beats per minute. This was the lowest count obtained for Atwater on that day. Lowsley found that his subjects' pulse rate after exhaustive exertion returned to normal in about three and one-half hours. The evening meal again accelerated Atwater's heart so that seven hours after the accent the rate was 93.

We started to take Gregg's pressure nine minutes after arrival on the summit. He felt slightly uncomfortable at the time and yet to our surprise he fainted immediately after the systolic pressure of 94 mm. had been determined. Previously by the rough procedure of raising and lowering the hand while a superficial vein was watched it had been noted that his venous pressure was negative. Immediately after Gregg fainted we placed him on a bed where he at once revived. He fainted at 12.54 p.m. and on recovery two minutes later his heart rate was 102 beats per minute. Four minutes later his systolic pres-

sure was 94, diastolic pressure 78, and pulse pressure only 16 mm. Hg. He rested on the bed much of the afternoon. The pulse pressure gradually improved throughout the next hour, reaching at the end 35

TABLE IV

Effects of walking up Pike's Peak

TIME	PULSE RATE	ARTERIAL PRESSURE IN MM. Hg			VENOUS PRESSURE IN CM. H_2O	REMARKS
		Systolic	Diastolic	Pulse		
(Atwater)						
Average.....	64	138	90	48	7.8	Colo. Springs.
12.46 p.m.....	114	146	94	52		Pike's Peak, arrived at 12.44 p.m.
12.50 p.m.....	114	144	93	51	10.9	
1.15 p.m.....	102	131	94	37	8.7	
1.35 p.m.....	108	126	92	34		
2.05 p.m.....	93	135	92	43		
3.00 p.m.....	90	130	89	41	2.2	
4.00 p.m.....	90	132	90	42	−4.2	
5.00 p.m.....	84	140	97	43	−3.0	
7.45 p.m.....	93	140	105	35		
(Gregg)						
Average.....	71	115	84	31	11.5	Colo. Springs.
12.54 p.m.....		94			Negative	Pike's Peak, arrived at 12.44 p.m.
12.56 p.m.....	102					Just recovered from fainting.
1.00 p.m.....	108	94	78	16		
1.06 p.m.....	108	100	80	20		
1.12 p.m.....	108	100	79	21		
1.25 p.m.....	102	102	74	28		
1.45 p.m.....	102				Negative	
1.55 p.m.....	102	114	79	35		
3.05 p.m.....	108	116	79	37		
5.15 p.m.....	96	112	79	33	−1.6	
7.35 p.m.....	102	120	93	27		

mm. which was somewhat above normal, this being 31 mm. in Colorado Springs. This change in pulse pressure was wholly the result of an improvement in the systolic pressure which increased from 94 to 100

mm. in six minutes, and then more gradually to 114 mm. Gregg's averages in Colorado Springs were: systolic 115, diastolic 84, pulse pressure 31 mm. Hg, and venous pressure 11.5 cm. of water. For at least four and a half hours after the ascent Gregg's diastolic pressure was subnormal. The return of the systolic pressure to normal, therefore, raised the pulse pressure a few millimeters above normal.

The venous pressure remained negative throughout the day and the pulse rate high; the lowest count, four and a half hours after he arrived, was 96.

One of Mosso's (7) soldiers, on Monte Rosa, fainted after lifting two five-kilogram dumb-bells 150 times. Mosso was able to study the respiratory changes in detail and also counted the pulse rate. He reported that the respiratory and cardiac functions were contemporaneously modified. Six minutes had passed after the cessation of work before his subject manifested any weakness in the functions of the heart and breathing apparatus. The heart rate had fallen from 136 to 120 beats per minute at the beginning of the faint. On recovery it was only 104 per minute. Gregg's heart rate after recovery increased from 102 to 108 per minute where it remained for about twenty minutes. The delay in the onset of the attack of fainting, as was observed by Mosso and by ourselves on Gregg, is not unusual. After severe muscular work the physical condition of the worker may become worse for a time.

Gregg ate a light supper which sent his systolic pressure to 120 and his diastolic pressure to 93 mm., resulting in a fall in pulse pressure. The result of the evening meal for both Atwater and Gregg was a marked fall in the pulse pressure, associated in each case with a rise in the diastolic pressure. The heart rate accelerated for both men.

Unfortunately, because all members of the expedition were more or less incapacitated by the altitude and fatigue, the circulatory changes in Eager, Havens, and Munro were not carefully followed after their walk up the Peak. They arrived at 4 p.m. Eager's pulse rate was then 136 and three hours later had retarded only to 115 beats per minute. Havens at 4.30 p.m. had a rate of 128, at 7 p.m. it was 96, and at 8.30 p.m. had retarded to 82 beats per minute.

It is clear from our observations on these men who walked up the mountain, as is shown by the long subnormal period of the arterial pressure and in the prolonged high rate of heart beat, that the exertion is very exhausting and puts a serious strain upon the heart.

CONCLUSIONS

The normal circulatory conditions for the majority of men at an altitude of 14,109 feet are an increased rate of the heart beat, an unchanged or slightly lowered arterial pressure, and a lowered venous pressure. Physical exertion, as at a low altitude, affects all three, the pulse rate is further accelerated, the arterial and venous pressures are both raised, however, the change in each is substantially greater at the high altitude. Furthermore the stimulating influence of lowered barometric pressure is the more pronounced the more vigorous the exertion, that is to say, the curves representing the acceleration of the heart rate and the increase in pressures rise more rapidly than the curve that expresses the addition in rapidity or vigor of exertion. These facts clearly show that the heart and blood vessels, the arteries but not the veins, in that the venous pressure rarely goes above the low altitude average, undergo a greater strain during exertion at the high altitude than they experience for the same form of exercise at the low altitude. The irritability of the circulatory mechanism during and immediately following physical work is greatest throughout the first days spent on the heights; it decreases, particularly during moderate exertion, as the bodily changes of acclimatization progress. For persons in excellent physical condition and who have reacted well to the altitude, the changes of acclimatization will permit of moderate exertion without the lowered barometric pressure manifesting itself by the more pronounced acceleration of heart rate and in increased pressure. It seems probable that in vigorous work even those who are best adapted to the high altitude will continue to give a more pronounced reaction than would occur at a low altitude.

That the above is a fair statement of facts is evidenced by the following points taken from our experiments. The muscular action required for standing, as determined by the difference in the number of heart beats between the standing and reclining postures, did not even during the first days of residence at the high altitude very materially accentuate the heart rate acceleration. The three-mile per hour walks at the low altitude resulted in the following average changes for Cheley: pulse 11 beats, systolic 0 mm., and diastolic 0 mm. Hg; the first day spent on Pike's Peak the increase was pulse 34 beats, systolic 28 and diastolic 4 mm.; on the fourth day pulse 26 beats, systolic 8 and diastolic 0 mm. Schneider in eleven days fully returned to his low altitude reaction. The four-mile per hour walk gave for Cheley the fol-

lowing reactions: average increase in Colorado Springs pulse 24 beats, systolic 6 and diastolic 1 mm. Hg; first day on Pike's Peak pulse 61 beats, systolic 44 and diastolic 7 mm.; fourth day pulse 54 beats, systolic 23 and diastolic 4 mm. Three men remained for two weeks on the summit but did not fully recover the low altitude reaction although they showed marked improvement. One man, however, who was in excellent physical condition had about the same increase in heart rate at the two altitudes. In two weeks residence three subjects showed no improvement in the amount of the reaction following the short quick runs. The acceleration of the pulse rate and the increase in systolic pressure were enormous and corresponded to the changes others have noted in the most exhaustive types of exercise at low altitudes.

That the heart undergoes greater strain during exercise at the high altitude is also indicated in the longer after period of high rate of beat and high pressures and also in the prolonged subnormal period of systolic pressure. This subnormal period after the short quick runs was as prolonged as Lowsley found after exhaustive exercises.

Our observations show clearly that physical exertion makes greater demands on the heart and blood vessels at very high than at low altitudes. They also indicate that during the first days of residence at the high altitude physical work should be reduced to a minimum. The writer has seen two persons faint just after arriving on the summit because they ran, to escape rain, from the train into the restaurant. The reason is quite evident. It is apparent that it would be an easy matter to seriously injure the heart during the early days of residence at the high altitude. For persons untrained and unaccustomed to physical work the climb to the summit of such a mountain as Pike's Peak must mean a serious strain for the heart. Ravenhill (14) cites two deaths from the cardiac type of mountain sickness of men who underwent considerable exertion in ascending a mountain in the Andes to an elevation of 15,400 feet. He found that men who did not remain quiet the first day or two at that altitude almost invariably became mountain sick. That the risk to the heart is less for men who are physically strong because of athletic training is indicated by the way Havens reacted to exercises at the high altitude.

It is to be expected that living at a high altitude, especially when much physical work is done, might increase the weight of the heart, for all muscular exertion tends to increase the weight of the heart and the result of work at the high altitude would accentuate the tendency.

Strohl (15) compared the heart of the alpine snowbird (Lagopus mutus) which ranges from an altitude of 6700 to 10,000 feet with the moor snowbird (Lagopus lagopus) which is not found above 2000 feet and found that the average weight of the heart for each 1000 grams of body weight was for the Alpine bird 16.30 and for the Moor bird 11.08 per cent. The hypertrophy of the right was greater than that of the left ventricle. Heger and Meyer (16) studied the hearts of guinea pigs and rabbits at two altitudes, by weighing and with the orthodiagraph, and found the hearts of the rabbits at the high altitude larger. Stohl made one observation of considerable interest in which he found that the heart of a young Alpine snowbird one and one-half months old had the same proportions in weight as that of the Moor snowbird, which suggests that the differences ordinarily observed at the two altitudes are due to greater muscular activity at the high altitude.

There is nothing in our work to show why the right ventricle should hypertrophy more than the left. We noted, however, that Zuntz and Schumburg (17) found in their study of the influence of marching on the heart that the right ventricle was dilated on sixty-two occasions while the left was involved only thirty-one times.

SUMMARY

1. (a) By the first morning spent at the high altitude the pulse rate had accelerated in the group that ascended by train and remained well to from 4.5 to 15.6 per cent, in the mountain sick group to from 22.4 to 46.6 per cent, and for those who walked up to from 26 to 66 per cent. The mean pulse rate showed the same group differences, while the variations throughout the day were the same for each.

(b) The frequency of the heart beat due to changes in posture was not materially different at the two altitudes.

(c) The observations on the after effects of walks for fifteen minutes at the rate of three and four miles per hour and of a short rapid run show that physical exertion accelerated the heart rate more at the high than at a low altitude, and that the altitude influence was disproportionately increased as the amount of work was increased. For moderate exertion the effects were greater during the first days of residence. After a time the three-mile walk did not call forth the altitude acceleration, but it persisted after the four-mile walk even after two weeks of residence. The time required for the heart rate to return to normal was also prolonged during the first days but was reduced with acclimatization.

The short rapid runs were exhausting at the high altitude, the heart was accelerated on an average of 120 beats per minute and the rate remained high for several hours thereafter.

(d) During work on a stationary bicycle at the high altitude the heart rate increased to the maximum in the primary rise; while at the low altitude the maximum came later, in the secondary rise.

2. (a) The three arterial pressures were higher after a given form of work at the high than at the low altitude. The influence of lowered barometric pressure was the more pronounced the more vigorous the exertion. The reaction was most conspicuous during the first days of residence, but while lessened by acclimatization it did not wholly disappear after a residence of two weeks. The average rise in the systolic pressure after a short quick run was 61 mm., while the average pressure for each of three men was 177, 195, and 197 mm. Hg. These high pressures were similar to those caused by a maximum lift of weights. The delay in the return to normal was as prolonged as after exhaustive exercises.

(b) During work the arterial pressures rose more rapidly at the high than at a low altitude, the rate of rise was not as rapid as that of the pulse rate. Ordinarily at the low altitude the arterial pressure reaches its maximum before the pulse rate, but at the high altitude the pulse rate first comes to the maximum.

3. Physical work caused in five out of seven subjects a greater rise in the venous pressure at the high than at the low altitude. The maximum, however, was on the average less than at the low altitude because of the fact that the normal venous pressure was lower on Pike's Peak.

4. The exertion of walking up the Peak is shown to be exhausting and to put a serious strain upon the heart.

The writer wishes to thank generous friends who contributed toward the expenses of the expeditions to Pike's Peak. He is also indebted to the young men who so kindly served as subjects for these observations.

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THE APPEARANCE OF SUGAR IN THE SECRETIONS OF THE DIGESTIVE TRACT FOLLOWING THE ADMINISTRATION OF PHLORHIZIN

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Since v. Mering discovered in 1886 that the administration of phlorhizin renders an animal glycosuric, many attempts have been made to learn the nature of the phlorhizin effect. The article on "Phlorhizin Glycosuria" by Graham Lusk which appeared in the "Ergebnisse der Physiologie, 1912" contains a complete review of the literature on this subject, hence, only a brief statement of previous work which bears on the present communication need be given here.

It is generally accepted that the glycosuria following phlorhizin administration is accompanied by a hypoglycaemia, and that this serves to differentiate it clearly from other forms of glycosuria, in which a state of hyperglycaemia exists. Because the injection of phlorhizin into the renal artery is immediately followed by a glycosuria, and since no reduction occurs in the amount of blood-sugar in phlorhizinized animals, in whom the renal arteries or urethers have been tied, most physiologists have concluded that phlorhizin exerts a specific action on the renal cells, producing what might be termed a "renal diabetes." There have been several hypotheses advanced to explain the mechanism of phlorhizin glycosuria. The "vehicle theory" proposed by Minkowski, assumes that phlorhizin, being a glucoside composed of a glucose molecule and a substance known as phloretin, is broken down by the kidney cell into its constituent parts of which the sugar escapes into the urine, whereas the phloretin recombines with sugar brought to the renal cells by the blood to reform phlorhizin which again breaks down: and so the process goes on till finally the phlorhizin is completely excreted from the body. Another theory supported by the experimental data of Levene, Biedel and Kolisch, Pavy and Lepine, is that the renal cells under the influence of phlorhizin bring about a change in the blood-sugar which makes it diffusible and enables it to pass through the renal epithelium into the urine.

Underhill, using maximal phlorhizinized dogs, found that an increase in blood-sugar resulted when the kidneys of the dog or rabbit were thrown out of function. This hyperglycaemia is not as great as in the depancreated animal, yet it indicates a specific stimulation of sugar production by phlorhizin. Underhill, nevertheless, recognizes a specific renal action in phlorhizin (1).

The explanation accepted by most physiologists is that phlorhizin specifically affects the renal cells either to increase their permeability to blood-sugar or to excite them to secrete dextrose.

All the hypotheses of phlorhizin action assume a specific action of the drug on the kidney. There are some observations, however, which point to the possibility of its having a more general action. In 1894 Levene found that a reducing substance is present in the bile of phlorhizinized animals, whereas none is found in the normal bile. Brauer, using a different method to free the bile of pigments, was unable to confirm this finding. Ray, McDermott, and Lusk could not detect any sugar in the bile vomited by phlorhizinized animals. Recently, Woodyatt has repeated the examination of the bile as directed by both Levene and Brauer, and has succeeded in showing that if the bile is properly prepared it will ferment with yeast and yield characteristic dextrosazone crystals (2).

Cornevin believed that phlorhizin has a direct action on the mammary gland but this work has not been confirmed by subsequent workers. Delmare reported the presence of a reducing substance in the sweat of a phlorhizinized animal. This work has never been repeated. Aside from those above mentioned, no attempts have been made to discover whether or not phlorhizin directly affects secreting glands other than the kidney.

DISCUSSION OF RESULTS

In the present research I have investigated the reducing power of the pancreatic, gastric, and salivary secretions in normal and phlorhizinized dogs.

The pancreatic juice

The experiments on the pancreatic juice were performed on dogs which had been starved for two or three days before the operation. The juice was collected from a cannula inserted in the pancreatic duct, and the pancreas was stimulated by the intra-venous injection of secretin, prepared as directed by Bayliss and Starling. In a few cases in

which the amount of juice obtained by the action of the secretin was small, pilocarpin was given, but it failed to excite secretion in all but one experiment.

Samples of blood for blood-sugar estimations were taken at frequent intervals before and after the injection of the secretin. The pancreatic

TABLE 1

The sugar content of the pancreatic juice of normal dogs to which phlorhizin had been given two hours before the experiment

NUMBER OF EXPERIMENT	DATE	NORMAL OR PHLORHIZINIZED ANIMAL	STARVATION PERIOD IN DAYS	CUBIC CENTIMETERS OF JUICE OBTAINED	NYLANDER'S TEST	BENEDICT'S TEST	PICRIC ACID REDUCTION TEST	PER CENT OF SUGAR IN THE PANCREATIC JUICE	PER CENT OF SUGAR IN THE BLOOD BEFORE THE INJECTION OF SECRET.N	PER CENT OF SUGAR IN THE BLOOD AFTER THE INJECTION OF SECRETIN
1	10/26	Phlorhizin	2	25	+	+	+			
2	10/28	Phlorhizin	3	10	+			0.07	0.076	0.075
3	11/1	Phlorhizin	2	7		+	+	0.09	0.12	0.122
4	11/3	Normal	2	12	0	0	0		0.125	0.120
5	11/6	Normal	2	10	0	0	0			
6	11/8	*Normal	2	6	0		0		0.105	0.105
8	11/11	†Phlorhizin	2	6		0	0		0.100	0.110
9	11/13	Phlorhizin	2	12		+	+	0.10	0.13	0.13
10	11/15	Phlorhizin	1			+?	+	0.05	0.127	0.13
11	11/16	Phlorhizin	2	8			+	0.04	0.08	0.08
12	11/16	Phlorhizin	2	12		+	+	0.066	0.08	0.08
14	11/24	Phlorhizin	2	3				0.085‡	0.085	0.10
17	12/8	§Phlorhizin	2	2			+	0.035	0.085	0.10
19	12/9	Normal	2			0	0		0.095	0.095
20	12/10	Normal	0	12		+	+	0.06	0.175	0.18

* Pilocarpin was given after secretin.

† Urine gave marked reduction.

‡ Peculiar color reading questionable.

§ Phlorhizin injected intravenously after taking sample of normal juice which gave no reduction.

juice, obtained from normal dogs and from dogs to which two gram doses of phlorhizin dissolved in 1.2 per cent sodium carbonate solution had been given subcutaneously two hours earlier, was tested for its reducing power by Benedict's and Nylander's tests. The protein was removed from the juice by colloidal iron and the clear filtrate was concentrated before applying the above tests. Since normal pancreatic juice does not

reduce the alkaline picric acid solution, quantitative estimations of the reducing power of the juice were made by the method proposed by Lewis and Benedict for the estimation of the blood-sugar. For the same reason also it is permissible to use this method as a qualitative test for the detection of a reducing substance in the juice after the administration of phlorhizin. This was done in a few cases in which the amount of juice was too small to permit of other tests being applied.

Table I gives the results of the experiments in which the dextrose content of the pancreatic juice of normal and phlorhizinized dogs was determined. It will be seen that the percentage of reducing substances in the juice is considerably lower than that of the blood at the same time. The injection of the secretin had apparently no effect on the amount of reducing substance in the blood, and the period of starvation previous to the experiment was evidently long enough to prevent a hyperglycaemia from developing during the anaesthesia.

Attention should be called to experiment 8 in which no reducing substance appeared in the pancreatic juice following the administration of phlorhizin. The urine was loaded with sugar at the time. I can offer no explanation for this negative result. Experiment 20 is also of interest since it shows the presence of sugar in the pancreatic juice of a normal dog whose blood showed a high percentage of sugar. This animal had not been starved.

A pancreatic fistula was made in one dog after the method devised by Pavlov. The juice obtained from the fistula after the injection of 50 cc. of 0.4 per cent hydrochloric acid into the stomach or after feeding with meat was found to be free from reducing substance. The juice obtained under similar conditions, but after the administration of phlorhizin gave reduction with both Nylander's and Benedict's tests, and dextrosazone crystals were obtained with the phenylhydrazine test. The amount of dextrose present in this juice was estimated to be about 0.035 per cent.

The gastric juice

The experiments on the gastric secretions were made on dogs possessing a Pavlov stomach.[1] The juice secreted by the small stomachs after feeding with meat, was collected hourly both under normal conditions and following the administration of phlorhizin, which was given, in 2 gram doses, dissolved in 1.2 per cent sodium carbonate solution.

[1] These were generously loaned me by Professors Carlson and Luckhart of the Physiological Laboratory of Chicago University, and I wish to express my thanks for the assistance given me by these gentlemen.

The amount of juice obtained in this way is usually small and it was therefore necessary to employ a test capable of detecting a low concentration of reducing substance in a small amount of fluid. Since normal gastric juice does not reduce the alkaline picric acid mixture as recommended by Lewis and Benedict for the estimation of blood-sugar, it was

TABLE 2

The reducing properties of the gastric juice of normal and phlorhizinized dogs

DATE	HOURLY SAMPLES	DOG B		DOG T		DOG C†	
		Qualitative dextrose test	Per cent dextrose	Qualitative dextrose test	Per cent dextrose	Qualitative dextrose test	Per cent dextrose
11/17	No. 1	0		0		0	
	Phlorhizin given						
	No. 2	+	*	+	0.03	+	*
	No. 3	+	0.025	+	0.025	+	0.035
	No. 4	+	0.035	+	*	+	*
	No. 5	+	*	0		+	*
12/3	No. 1	0		0		+	0.02
	No. 2	0		0		+	0.03
	Phlorhizin given						
	No. 3	+	0.033	0		+	0.05
	No. 4	+	0.04	+	0.038	+	0.06
	No. 5	+	0.04	+	0.03	+	0.045
12/13	No. 1	0	0	0		0	
	No. 2	0		0		0	
	No. 3	0		0		0	
	No. 4	0		0		0	
	No. 5	0		0		0	

† Dog C possessed a Heidenhain stomach.

* Denotes that enough juice was not obtained to make a quantitative sugar determination.

possible to use the reaction as a test for the appearance of reducing substance in the gastric juice following phlorhizin administration. The test is not specific for sugar and is perhaps faulty in other regards, nevertheless, it is so delicate that a very low percentage of a reducing substance can be detected in a very small quantity of fluid. The picric acid precipitates any mucus that may be present and the filtrate on boil-

ing with a little sodium carbonate solution turns red if a reducing substance is present. I have never observed a similar reaction in normal gastric juice but have obtained it quite uniformly in the gastric juice of dogs which were under the influence of phlorhizin. The gastric juice collected from a dog with a Heidenhain pouch, on one occasion, gave slight reduction with the above reagent. Its reducing power increased, however, when phlorhizin was given. A test made on a subsequent day failed to show reduction. The gastric juice from the Heidenhain pouch of a goat (which was kindly loaned me by Professor Carlson) reduced the picric acid reagent, but did not reduce Benedict's reagent. Phlorhizin did not produce any change in the juice of this animal in the one experiment.

The results of the experiments on the gastric juice are given in Table 2.

In each of the experiments, after a sufficient amount of the juice had been collected to make quantitative estimations of the reducing power, by means of the Lewis Benedict method, the remaining samples were combined and after freeing the mixed juice of mucus, the filtrate was concentrated and tested with Benedict's reagent. Reduction occurred with the juice obtained while the animals were under the influence of phlorhizin. These results indicate that phlorhizin affects the gastric glands in the same way as it affects the pancreas.

The saliva

Some of these experiments were done on the same animals that were used in the experiments on pancreatic secretion. In such cases the saliva was obtained before the administration of the secretin. The submaxillary gland was made to secrete by stimulation of the chorda tympani and the saliva was collected by means of a cannula inserted into Wharton's Duct. The reducing power of the saliva of normal dogs and of animals poisoned with phlorhizin was tested as in the experiments on the gastric and pancreatic juice. In the saliva of normal dogs I have never found sugar save in one case (experiment 20) in which the blood-sugar was 0.18 per cent. The amount present in the saliva in this case was estimated at about 0.04 per cent and it is important to note that the pancreatic juice of this dog also reduced Benedict's reagent. This finding is in harmony with the discovery by Carlson and Ryan that the saliva of cats under ether anaesthesia may contain sugar (3).

The figures in table 3 give the results of the experiments. Out of nine experiments five are absolutely negative. Two of these are ex-

periments in which sugar was found in the pancreatic juice. In the positive experiments the amount of reducing substance in the juice was very small. The fact that I found reducing properties in the juice of some phlorhizinized animals and did not find them in normal animals with normal blood-sugars is, I believe, significant.

In order to determine whether the action of phlorhizin on the various glands of the body is independent of its action on the kidney, I ligated the renal vessels in two dogs previous to the administration of the drug. Pancreatic juice subsequently obtained was examined for its reducing power. In one experiment in which a good flow of juice was obtained reduction occurred with Benedict's reagent. In the other experiment

TABLE 3

The influence of phlorhizin on the reducing properties of saliva. Obtained from a cannula in Wharton's duct of a dog

NUMBER OF EXPERIMENT	DATE	STARVATION PERIOD	PICRIC ACID TEST	BENEDICT'S TEST	PER CENT REDUCING SUBSTANCE IN SALIVA	PER CENT DEXTROSE IN BLOOD
2	10/28	3	0	0		0.075
3	11/1	2	0	0		0.12
12	11/16	2	+	+	0.02?	0.08
14	11/24	2	0			
17	12/8	1	+		0.035	0.08
21	12/10	0	+		0.037	0.13
22	12/11	2	+	+		0.085
23	12/14	2	+		0.03	
24	12/14	2	0			

sufficient juice only was obtained to make a qualitative test by the picric acid method, the result being positive.

The results of these experiments taken along with the observations of previous investigators of the presence of sugar in the bile and sweat of phlorhizinized animals, indicate that phlorhizin does not act on the renal cells alone. It is true that sugar is found in far greater concentration in the urine during phlorhizin poisoning than in the blood or in the above mentioned secretions, but the same is true of the glycosuria produced by the hyperglycaemia following pancreatectomy and the intra-venous injection of sugar. In one case in which I injected sufficient sugar into the femoral vein to produce a hyperglycaemia of 0.5 per cent the urine contained over 4 per cent of sugar and the pancreatic juice obtained a few minutes later, contained 0.33 per cent of reducing sub-

stance. In this case it would hardly be thought that the sugar acts on the kidney in a different way than on the pancreas. The method by which the kidney concentrates the sugar in the urine may very well be the same in the glycosurias which follow phlorhizin poisoning and in those which depend on hyperglycaemia.

The fundamental nature of the action of phlorhizin is still unknown. The blood-sugar, as suggested by Woodyatt (4) may be considered as being in a state of equilibrium with the sugar of the cells and this again with sources (glycogen and protein) from which it may be formed.

In other words, we may think of the sugar as exerting a partial pressure in all the cells and fluids of the body just as do O_2 and CO_2. Any factor which reduces the partial pressure in one locality will eventually reduce its pressure in all parts of the body. Phlorhizin produces a change in the partial pressure of the sugar in the body, as it were, and wherever sugar can escape it does so. The chief expression of the phlorhizin action is in the kidney because in this organ there is a highly developed mechanism for the concentration of substances excreted from the blood into the urine. The methods by which phlorhizin makes the kidney cells, and the cells of other secreting glands permeable to sugar are, no doubt, alike.

SUMMARY

The normal pancreatic, gastric, and salivary juices of the dog do not contain an appreciable amount of reducing substance. The pancreatic and gastric juices and sometimes the salivary juice of dogs rendered glycosuric by phlorhizin, contain a reducing substance. In the case of the pancreatic juice, this has been shown to be dextrose.

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THE DESTRUCTION OF HORMONES, PROENZYMES AND ENZYMES BY ULTRA-VIOLET RADIATION

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During the past decade several observers have exposed enzymes to ultra-violet radiation and determined the relation between the length of time of exposure and the decrease in the activity of the enzymes. Dreyer and Hanssen (1) showed that the destruction follows the law for unimolecular reactions. Schmidt-Neilson (2) using a 1 per cent solution of rennin came to the same conclusion regarding the destruction by ultra-violet radiation. Green (3) was among the first to show the destructive effect of the short wave lengths of the spectrum on enzymes. It has been recognized in photography since the time of Bunsen and Roscoe that the relation between the exposure of silver salts to light and the amount of silver reduced by the action of light without further treatment is linear, that is, the mass of silver reduced is proportional to the energy applied. According to Faraday's law the amount of silver deposited upon the cathode, when an electric current is passed through a solution of silver salt, is proportional to the amount of current passed, that is, to the energy applied. It has been shown that this same relation exists between the amount of current passed and the destruction of enzymes (4). In view of these facts it would seem that the relation between the decrease in enzyme activity and exposure to ultra-violet radiation should be linear. The experiments reported in this paper were carried out to see if this was true.

Method. Five cubic centimeters of the solution to be exposed were introduced into a circular glass vessel 5 cm. in diameter and 1 cm. deep. This was covered during the exposure with a quartz plate 2 mm. thick and partially immersed in running water under a quartz mercury-vapor burner operating at 140 volts, 3.3 amperes, 2400 cp. Previous to the exposure the solutions were made perfectly clear by filtration. Colored solutions were rendered colorless by filtering through a thin layer of animal charcoal.

HORMONES

Adrenalin. A colorless commercial preparation of adrenalin chloride was diluted 1 to 15 with distilled water. Five cubic centimeters of the clear solution were introduced into the glass vessel and exposed to the radiation for 20 minutes at a distance of 5 cm. This was removed and another 5 cc. was introduced and exposed for 40 minutes. Similarly another 5 cc. was exposed for 60 minutes. Three cubic centimeters of the unexposed solution were injected into the jugular vein of an etherized dog while the arterial pressure was being recorded by means of a mercury manometer. After the blood pressure had returned to normal 3 cc. of the solution exposed for 20 minutes were injected. Similarly 3 cc. of the solutions exposed for 40 and 60 minutes respectively were

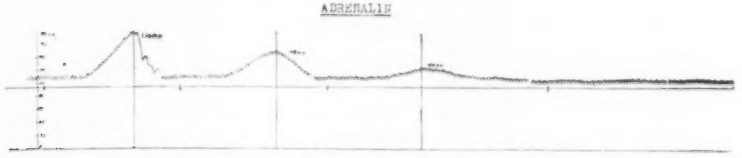

Fig. 1. The destruction of adrenalin by ultra-violet radiation. At *a*, 3 cc. of unexposed solution were injected; at *b*, 3 cc. previously exposed for twenty minutes; at *c*, 3 cc. previously exposed for forty minutes; at *d*, 3 cc. previously exposed for sixty minutes.

Length of Exposure	*Rise of Blood Pressure in mm. Mercury*	*Decrease in rise of Blood Pressure per 20' intervals of exposure of Adrenalin*
0	66	28
20	38	28
40	10	
60	0	

injected. The blood pressure records may be seen in figure 1. At *a*, 3 cc. of the unexposed adrenalin solution were injected; at *b*, 3 cc. of the solution previously exposed for 20 minutes; at *c*, 3 cc. previously exposed for 40 minutes; at *d*, 3 cc. previously exposed for 60 minutes. The injection of the unexposed solution caused a rise in blood pressure of 66 mm. of mercury; the solution exposed for 20 minutes caused a rise of 38 mm. of mercury; that exposed for 40 minutes a rise of 10 mm. of mercury, and the solution exposed for 60 minutes caused no rise in the blood pressure. The destructive effect on adrenalin of the 20 minute exposure is represented by the difference in the rise of blood pressure between 66 and 38 mm. Hg. or 28 mm.; that of the 40 minute exposure

by the difference between 66 and 10 mm. Hg. or 56 mm. which is also a decrease of 28 mm. per 20 minute interval of exposure. In all 10 experiments similar to the one described were performed. In three of these the rate of destruction of the adrenalin was absolutely proportional to the length of exposure, while the remaining seven deviated from absolute proportionality by 5 to 15 per cent.

Secretin. This was prepared by boiling the hashed mucosa of the intestines of dogs or of cattle with 0.4 per cent hydrochloric acid, the acid extract was neutralized while boiling with 1 per cent sodium hydroxide and filtered. Five cubic centimeters of the clear filtrate were introduced into the glass vessel and exposed to the radiation from the burner for 30 minutes at a distance of 5 cm. This was removed and replaced by 5 cc. of fresh solution which was exposed for 60 minutes. Similarly solutions were exposed for 90, 120, 150, and 180 minutes. Four cubic centimeters of each of the solutions thus exposed were injected into the jugular vein of an etherized dog and the number of drops of pancreatic juice caused to flow in five minutes beginning with the time of the first drop were counted. Previous to the injection of each exposed solution an injection of 4 cc. of the unexposed solution was made to serve as a control. The effect of the unexposed solution was always permitted to wear off before the injection of the exposed solution took place. In Table I it may be seen that in the 5-minute interval

TABLE I

Rate of destruction of secretin by exposure to ultra-violet radiation

Secretin

LENGTH OF EXPOSURE	NUMBER OF DROPS SECRETED IN FIVE MINUTES	DECREASE IN NUMBER OF DROPS SECRETED PER THIRTY MINUTE INTERVALS EXPOSURE OF SECRETIN
minutes		
0	15−	
30	12−	3
0	14	
60	10−	2
0	16−	
90	8+	2
0	15−	
120	6−	2+
0	14−	
150	3−	3
0	15	
180	0	3−

after the injection of the solutions of secretin previously exposed for 30, 60, 90, 120, and 180 minutes respectively, 12−, 10−, 8+, 6−, 3−, and 0 drops of pancreatic juice were secreted. It may also be seen that the control for each of these solutions shown after 0 time exposure were fairly constant being 15−, 14, 16−, 15−, 14− and 15 drops of pancreatic juice secreted in the 5-minute intervals. The table also shows that the rate of decrease in the activity of the secretin is represented by a decrease in the flow of pancreatic juice of approximately 2 drops for each 30-minute interval of exposure of the secretin. Six experiments similar to the one described were carried out with comparatively little difference in the results.

Cholagogues. The gall bladder of a dog was tied off and a cannula was introduced into the common bile duct. Fifty cubic centimeters of bile were collected as the result of repeated injections of ox bile into the jugular vein. The bile was filtered through a thin layer of animal charcoal and rendered somewhat more colorless than the original bile. Five cubic centimeters of the filtered bile were exposed to the radiation from the quartz mercury-vapor burner in the glass vessel at a distance of 5 cm. for 10 hours. Four cubic centimeters of the unexposed bile were injected into the jugular vein of a dog having a cannula in the common bile duct. The rate of flow was increased by the injection of this amount of the unexposed bile from 5 drops to 20 drops in the 5-minute interval after the injection beginning with the time of the first drop. Four cubic centimeters of the bile exposed for ten hours were injected. This increased the rate of flow from 4 drops to 18 drops in the 5-minute interval after the injection. From the results of this typical experiment it may be concluded that exposure to ultra-violet radiation has no effect on the cholagogic properties of bile. Cholic acid prepared according to the method of Plattner was tried in the same manner as the bile with a similar result.

ENZYMES AND PROENZYMES

Trypsin and Trypsinogen. One hundred cubic centimeters of clear pancreatic juice were collected from the cannula in the pancreatic duct of a dog as the result of the repeated injections of secretin into the jugular vein. This amount was divided into two portions of 50 cc. each. To one portion 2 cc. of enterokinase were added. This 50 cc. was the solution of trypsin used in the experiments to be described and the remaining 50 cc. the trypsinogen solution used.

Six portions of 5 cc. each of the trypsin solutions were introduced into the glass vessel and exposed to the radiation at a distance of 10 cm. for 10, 20, 30, 40, 50, and 60-minute intervals respectively. Mett's tubes made of 10 per cent gelatin colored with congo red were placed in the solutions thus exposed and permitted to digest for 24 hours at 20°C. In figure 2 under "trypsin" is shown a photograph of the tubes of a typical experiment. Tube "n" had been in the unexposed solution, tubes 1, 2, 3, 4, 5, and 6 had been in the solutions exposed to the radiation for 10, 20, 30, 40, 50, and 60-minute intervals respectively. The light portion of the tubes represents the extent of digestion, the dark portion the undigested gelatin. It may be seen that the tryptic activity is decreased by exposure to the radiation and that the rate of this decrease is proportional to the length of time of exposure.

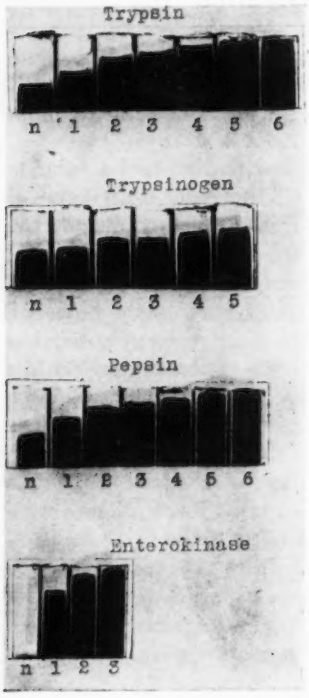

Fig. 2. The destruction of trypsin, trypsinogen, pepsin, and enterokinase by exposure to ultra-violet radiation.

The trypsinogen solution was exposed to the radiation as the trypsin had been. Two drops of enterokinase were added to 3 cc. of each of the exposed solutions and to 3 cc. of the unexposed solution. Mett's tubes were introduced into the solutions. After the digestion had proceeded at room temperature for 24 hours the tubes were photographed (see fig. 2 under "trypsinogen.") The rate at which the trypsinogen is destroyed by the radiation is much slower than that of the trypsin. The trypsin was completely destroyed after 60 minutes exposure while the exposure of the enzyme in the zymogen state for the same period of time decreased its activity about 50 per cent.

Pepsin. Two grams of a commercial preparation of pepsin were dissolved in 100 cc. of distilled water. This solution was filtered and portions of 5 cc. each of the clear filtrate were introduced into the vessel

and exposed at a distance of 5 cm. for 10, 20, 30, 40, 50, and 60-minute intervals respectively. Two cubic centimeters of each of the exposed solutions and 2 cc. of the unexposed were acidified with hydrochloric acid to the extent of 0.3 per cent. Mett's tubes, made of egg white, were introduced into the solutions and the preparations were placed in a thermostat at 38°C. for 24 hours. In figure 2 under "pepsin" is a photograph of the tubes. It may be seen that the peptic activity was decreased by the exposure and that the rate of this decrease was proportional to the length of time of exposure.

Enterokinase. The mucosa of intestines of dogs as well as of cattle was gently scraped with the handle of a scalpel. This scraping was extracted with 0.9 per cent sodium chloride, centrifugalized and filtered until clear. Portions of 5 cc. each of the clear filtrate were introduced into the glass vessel and exposed to the radiation at a distance of 5 cm. for 2, 4, and 6-minute periods. Four drops of the unexposed enterokinase were introduced into a tube containing 2 cc. of trypsinogen. Similarly 4 drops of the solutions exposed for 2, 4, and 6 minute periods were introduced into tubes containing 2 cc. each of trypsinogen. Mett's tubes made of gelatin were introduced into the solutions and allowed to digest at room temperature for 24 hours. In figure 2 under "enterokinase" is a photograph of the tubes. The power of the enterokinase to activate trypsinogen was entirely destroyed after 6 minutes' exposure to the radiation.

Ptyalin. Fifty cubic centimeters of fresh saliva were centrifugalized and filtered until clear. Portions of 5 cc. each were exposed to the radiation at a distance of 5 cm. for 10, 20, 30, 40, 50 and 60 minute intervals. Two cubic centimeters of the unexposed solution were added to a 2 per cent starch paste at 38°C. The preparation was allowed to remain in the water bath at this temperature for 10 minutes. The solution was then boiled and the amount of sugar determined by Pavy's method. The amount of sugar produced by the action of 2 cc. of each of the exposed solutions was determined in a similar manner. The results of a typical experiment may be seen under "ptyalin" in Table II.

Amylopsin. Experiments similar to those made upon saliva were carried out with a clear solution of pancreatic juice collected from a dog. In Table II under "amylopsin" are given the results of a typical experiment.

It may be seen that the activity of ptyalin and of amylopsin is decreased by exposure to ultra-violet radiation and that the rate of this decrease is about 20 per cent per 5-minute interval of exposure for the ptyalin and per 10-minute interval of exposure for the amylopsin.

TABLE II

The destruction of ptyalin and amylopsin by ultra-violet radiation

LENGTH OF EXPOSURE	SUGAR PRODUCED BY ACTION OF PTYALIN	DECREASE IN ACTIVITY OF PTYALIN PER FIVE MINUTE INTERVAL OF EXPOSURE	SUGAR PRODUCED BY ACTION OF AMYLOPSIN	DECREASE IN ACTIVITY OF AMYLOPSIN PER FIVE MINUTE INTERVAL OF EXPOSURE
	mgms.	*per cent*	*mgms.*	*per cent*
0	17.4		14.0	
5	13.8	20		
10	11.0	19−	10.9	22
15	9.0	17−		
20	4.4	18+	7.9	22
25	2.5	17+		
30	1.7	15+	5.5	20
35	+	20−		
40	0.0		1.8	18
45				
50			+	20−

In all the experiments reported in this paper the substances were exposed in a glass vessel covered with a quartz plate. The substances were also exposed in the same vessel and under the same conditions except the vessel was covered with a clear glass plate 5 mm. thick instead of the quartz plate. When this was done none of the substances were affected after many hours exposure. It had been determined that the glass cover used did not transmit wave lengths shorter than 313 $\mu\mu$ hence these shorter wave lengths destroyed the substances exposed. It had also been determined that only wave lengths 302 $\mu\mu$ and 297 $\mu\mu$ in the spectrum of the quartz mercury-vapor burner used were effective in coagulating protein. It is reasonable to assume that these wave lengths caused the destruction of the substances exposed.

CONCLUSIONS

Hormones, proenzymes, and enzymes are destroyed by exposure to ultra-violet radiation. The rate of this destruction is proportional to the amount of energy applied. The specific wave lengths causing the destruction are 302 $\mu\mu$ and 297 $\mu\mu$. The cholagogic activity of bile is not affected by exposure to ultra-violet radiation.

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A NOTE ON THE EXCITATION OF THE PHRENIC NERVE BY THE ACTION CURRENT OF THE HEART

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The stimulation of the phrenic nerve by the action current of the heart has been seen by a number of investigators. Stewart and I observed some years ago that it was not necessary to open the chest cavity or to disturb the heart in any way in order to elicit contractions of the diaphragm at each beat of the heart (1). The interpretation placed upon our experiments at that time was that the change in excitability of the phrenic nerve due to changes in its blood supply, was the important element in the onset of its excitation by the action current of the heart. Our reasons for this view were:

1. That without any change in blood pressure or the relative positions of the heart and the phrenic nerves, the phenomena of excitation would appear.

2. In all experiments in which the phrenic nerve became excitable to the action current of the heart the blood supply of the upper portion of the phrenic nerve was cut off by ligation of the internal mammary artery at its source. The excitation of the nerve was manifested only some minutes after the artery was ligated. If the artery was occluded for a still longer time, the nerve again became inexcitable to the action current of the heart.

3. If the nerve had ceased to respond during the time the artery was occluded, it would again become excitable some time after the ligature was removed from the artery and the circulation to the nerve restored. The excitation would persist for a time and again cease as the nerve presumably more nearly approached its normal state, due to the access of oxygenated blood to it.

To these considerations we might add that in all of the cardiac conditions in which, as revealed by the electrocardiogram, there is any interference with the normal conducting mechanism of the heart or any disturbance of its electrical relations, excitation of the phrenic

nerve by the action current of the heart so far as my knowledge goes, has not been observed. In pericarditis with effusion, the short circuit for the action current of the heart is probably somewhat affected, the increased fluid perhaps providing a better return than usual. In some of the clinical conditions of the heart which have been investigated a worse short circuit for its action current, as Langendorff (2) suggested might be expected occasionally to occur. If this occurrence of a worse short circuit is the reason for the appearance of the excitation of the phrenic nerve by the action current of the heart, we would expect the twitching of the diaphragm to occur at times in clinical cases. It does not appear, therefore, that the change in the heart itself is the real condition, or, at least, the most important condition for the excitation of the phrenic by the action current of the heart.

The threshold value of stimulation of the phrenic nerve under ordinary normal conditions must be considerably above the ordinary effectiveness of the heart's action current, for twitching of the diaphragm is not observed in any cases of hypertrophy or in any other condition of the heart in which the magnitude of the action current is greater than normal.

I am, therefore, still of the opinion that the important element in the excitation of the phrenic nerve by the action current of the heart is the change in the excitability of the nerve itself. It seems probable that the accumulation of carbon dioxide may play the same rôle in increasing the excitability of the phrenic nerve that it does in the treppe of skeletal muscles (3). The inexcitability of the phrenic under all ordinary, and many extraordinary, conditions to the action current of the heart is a phenomenon so familiar as to escape comment. But one has only to reflect upon what life would be like if there were constantly present in the speech or song of all of us, abrupt, jerky tremors similar to those appearing in hiccough, to imagine some reason why the nerve is ordinarily inexcitable to the action current of the heart.

The new observation which is recorded here brings out, in what is to me a most instructive way, the difference in the speed of conduction of impulses in nerve tissue and in the heart itself. The diaphragm could be seen to contract before the ventricular systole became apparent to the eye. Perhaps other workers may be led to look for and record similar conditions.

January 19, 1916. A cat was used for a blood pressure experiment, but no drugs, aside from the ether for anaesthesia, were used. At the

close of the experiment, the trachea was clamped until the respiration stopped and the blood pressure fell very low. The respiration and heart beat did not start up again when artificial respiration alone was used, and the thorax was then opened. The heart was started by direct massage, after removal of the pericardial sac and clamping the thoracic aorta just above the diaphragm. The heart soon started under artificial respiration and direct massage, and the beat became strong and regular. The artificial respiration was then intermitted and the heart allowed to beat as long as it would. As the ventricular beats became slower, the auricular beats continuing at a greater rate than the ventricular, the left side of the diaphragm began to twitch at each beat of the ventricle. The heart was lying against the left phrenic nerve about 2 cm. above the diaphragm. The auricular beats were not sufficient to cause the twitching of the diaphragm, but only the ventricular beats. The diaphragm did not twitch on both sides, but only on the left. Nor did it twitch when the apex of the heart was moved over to the right side of the chest cavity, where it did not come in contact with the left phrenic nerve. The spontaneous beat of the ventricle was sufficient to excite the phrenic nerve, but the beat caused by touching the right ventricle with the point of a knife would not bring about any contraction of the left side of the diaphragm. The diaphragm could be seen to twitch strongly just before the systole of the ventricles became apparent to the eye. The interval was a fraction of a second, but long enough to admit of no doubt. The ventricular beats began to come in groups (Luciani's groups) toward the end, and the diaphragm showed a rhythm synchronous with that of the ventricles.

The tentative interpretation, for part of which I am indebted to Dr. H. B. Williams, is that the action current of the ventricles stimulated the left phrenic nerve. Owing to the fact that the action current precedes the sound of the heart due to the contraction of the ventricles one may suppose that the nerve was stimulated somewhat before the ventricular systole became apparent. The diaphragm reacts more quickly than the ventricular muscle, and the 2 cm. or so of phrenic nerve conducted the stimulus to the muscle more rapidly than the conducting substance in the slowly beating heart conducted the impulse to the ventricular muscle. The striking thing about the matter was the fact that the left side of the diaphragm twitched before the systole of the ventricles became apparent to the eye. The clamping of the

thoracic aorta, resulting in shutting off most of the blood supply of the lower part of the phrenic nerve, may have had something to do with its increased irritability.

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THE CHARACTER OF THE INNERVATION OF THE KIDNEY

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While the existence of vasomotor fibers to the kidneys needs no further confirmation, it seems desirable to ascertain whether the innervation of these organs is crossed or unilateral in character. By a series of quantitative measurements of the bloodflow through the left and right renal veins it has been established (1) that it is possible to markedly diminish the vascularity of the kidneys by the stimulation of the corresponding greater splanchnic nerve, as well as by the excitation of the plexus renalis and its single constituents. By the same method it has been found that the vagi nerves do not possess a vasomotor action upon the kidneys and that the renal plexus, in conjunction with the suprarenal plexus and the vagal terminals, forms the afferent path by means of which impulses gain the central nervous system.

Quite different results were obtained if the greater splanchnic nerve of the opposite side was subjected to the stimulation. At no time were we then able to incite such quick and powerful constrictor reactions as we had been able to get with the help of the preganglionic path of the same side. Thus, the stimulation of the right nerve usually led to a reduction in the vascularity of the left organ which set in only after a considerable latent period, was very variable in its amplitude and frequently disappeared long before the end of the excitation. Practically the same kind of differences were noted when the bloodflow through the right kidney was measured during the stimulation of the left nerve. It was also observed that these peculiar reductions in the renal bloodsupply were generally ushered in by rather brief augmentations in the flow. As the latter developed in strict accordance with the rise in the systemic blood pressure, they were attributed to the general vascular conditions and not to a local dilator action. All these changes, but especially the initial augmentor phenomenon, led me to believe that the direct vasomotor influence of the splanchnic nerve is restricted to the

organ of the corresponding side, and that therefore the innervation of the kidneys is unilateral in its character.

But while I clearly recognized at that time the different changes which occur under the experimental conditions just described, and while the conclusions drawn from them need no correction, I was much puzzled to find an explanation for the peculiar behavior of the kidney situated on the side opposite to the stimulation. In the last few years, however, certain data have been gathered regarding the function of the adrenal glands which, had they been obtained at a somewhat earlier date, would have greatly aided me in explaining my results. For this reason the plethysmographic experiments upon the kidneys dealt with in the succeeding pages, are intended to substantiate my earlier data and secondly, to bring them into relation with the more recent work upon the secretory activity of the suprarenal bodies.

Johansson (2) called attention to the fact that the elevation in the general blood pressure occasioned by stimulation of the splanchnic nerve, is not a simple rise and fall, but presents two summits. Bayliss (3), moreover, observed that the blood vessels of peripheral parts do not behave passively towards the changes in general blood pressure occasioned by the stimulation of the aforesaid nerve, but frequently display an independent constrictor action. Lehndorff (4) then offered the explanation that the first increase is caused by the constriction of the blood vessels innervated by the splanchnic nerve and the subsequent transfer of this mass of blood into the systemic circulatory channels. The second elevation he believed to be due partly to a greater force and frequency of the heart, and partly to a constriction of certain peripheral blood vessels. By extirpating the suprarenal bodies Elliott (5) succeeded in demonstrating that the second rise is dependent upon the outpouring of adrenalin into the circulation, the splanchnicus, as has been demonstrated by Asher (6), being the secretory nerve of this gland. The more recent experiments of von Anrep (7) have proved this conclusion to be correct, and have shown moreover that the stimulation of this nerve is also capable of inciting a constrictor reaction in the denervated kidney and hind-limb in an indirect manner by forcing a certain quantity of adrenalin into the circulation which finally enters the blood vessels of the passive organs.

The present experiments were performed upon dogs in ether narcosis. Both kidneys were enclosed in oncometers which were connected with recording pistons. The general blood pressure was registered by a mercury manometer which communicated with the left femoral artery.

Both thoracic sympathetic nerves were placed in shielded electrodes at a point directly above their division into the splanchnicus major and sympatheticus abdominalis. The intact nerves, as well as the distal ends of the divided nerves were employed. Naturally, this procedure necessitated the piercing of the diaphragm in the region of the crura and artificial respiration. The stimulations were indicated by a signal, while the time was registered in seconds by a Jaquet chronograph. All writing levers were adjusted in the same ordinate at the beginning of the experiment. In order to avoid possible conflicts, the zero-line of the blood pressure has not been recorded upon the paper.

The precedure followed in one series of experiments consisted in stimulating the right or left nerve at intervals with a current of moderate strength and duration, the endeavor being to obtain at least some reactions, which permitted of a comparison with others of the same amplitude. In another series of tests both nerves were stimulated simultaneously with currents of practically the same strength and duration, the individual reactions being incited at relatively long intervals so as not to exhaust the secretory power of the adrenals.

The accompanying figure 1 is intended to illustrate the changes in the volume of the kidneys following the stimulation of the left splanchnic nerve. The general blood pressure represented by the uppermost record, presents an elevation which is composed of two rises. The initial increase (to c) begins after a very brief latent period and gives way about 15 seconds later to a rise of still greater amplitude (after c). As has been stated previously, the first elevation is attributable to the vaso-constriction occurring in the different organs innervated by the aforesaid nerve, and the second, to a much more general constriction of the blood vessels caused by the discharge of adrenalin into the circulation. While the first effect appeared within a second or two after the onset of the stimulation, the subsequent elevation developed only after a well marked latent period, the average duration of which amounted to 12.8 seconds. Values between 10.4 and 16.2 seconds have been obtained, the time being practically the same for the two glands.

It is possible, however, to account for these variations without much trouble, because the circulation-time in different animals shows certain normal differences, and because the dynamical conditions constantly tend to become less favorable if the experiment is continued for a long period of time. For the same reason, the rapidity with which the adrenalin is discharged diminishes somewhat in the course of an experiment of this kind, and especially if the intervals between the

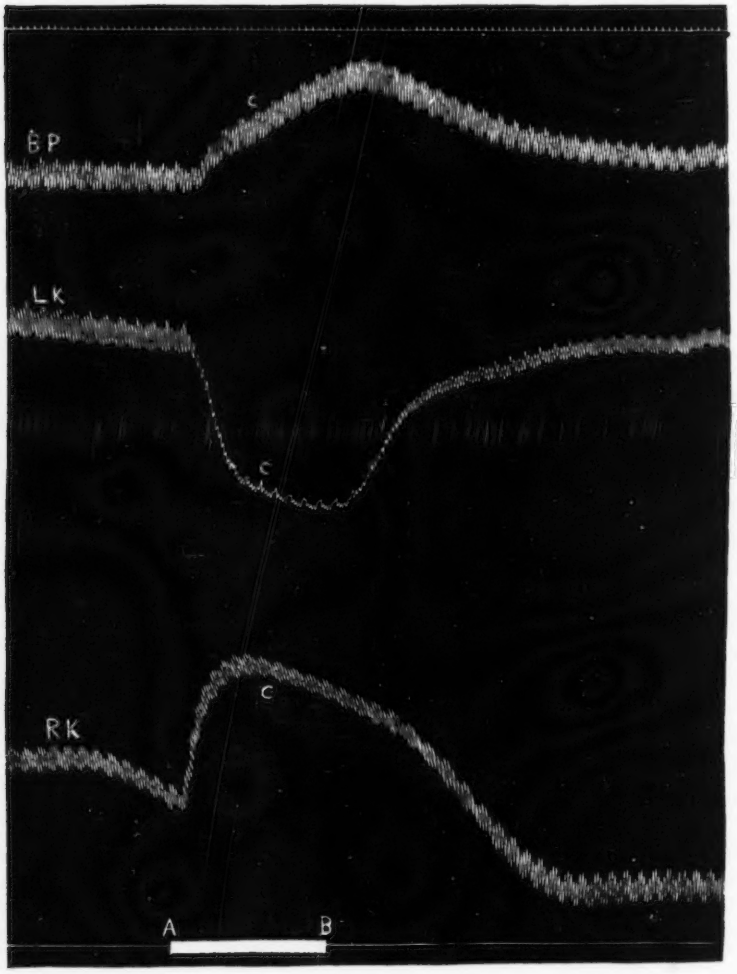

Fig. 1. Stimulation of the left splanchnic nerve (15 cm., 23 seconds)

stimulations are not sufficiently long to permit of a complete readjustment of the secretory power of these glands. Thus, it may happen that the second summit of the rise in the general blood pressure disappears entirely, while the first elevation, although of lesser amplitude, remains clearly in evidence.

By injecting minimal doses of adrenalin into the current of the portal vein in the vicinity of the hilus of the liver (8) I have found the circulation-time between this blood vessel and the systemic arterioles to be 14.1 seconds. In a similar way I have recently determined the time consumed in the passage of adrenalin from the renal and femoral veins to the distal arterial channels. In the former case, the average value obtained was 13.8 seconds and, in the latter, 16.4 seconds, these figures agreeing very well with the preceding value of 12.8 seconds for the circulation-time between the suprarenal veins and the arterial system.

The difference in time between the femoral vein, on the one hand, and the renal and suprarenal veins, on the other, amounts to about 2.6 seconds. In a dog weighing about 12.0 kg., the distance between the more peripheral blood vessel and the orifice of the renal vein measures approximately 17 cm. If now these two values are brought into relation with one another, it becomes evident that the blood progresses through the lower portion of the inferior vena cava and its iliac tributaries at the rate of about 65 mm. in a second.

In the curve represented by figure 1, the plethysmographic tracings of the kidneys are arranged below that of the blood pressure (B P), the one of the left organ (L K) being placed above that of the right (R K). The period of stimulation is indicated by the letters *A* and *B*. It is evident that the two records pursue at first a course in opposite directions to one another, the left kidney showing a decrease in its volume and the right organ an increase. Moreover, as these changes appear almost synchronously with the stimulation, they must be regarded as the direct results of the activity of the left splanchnic nerve. We know that this nerve exerts a vasoconstrictor influence upon the left kidney, and hence, it may justly be concluded that the fall in the oncometer record is attributable to a decrease in the vascularity of this organ.

The initial rise in the tracing of the right kidney shows first of all that the left splanchnic nerve possesses no direct vasomotor influence upon this organ, because under ordinary conditions of experimentation this nerve exhibits a constrictor tendency, and because it can readily be proved that this elevation has not been caused by vasodilator changes.

Thus, the deduction may justly be made that the right kidney remains passive at first, its increased volume being occasioned by the greater arterial influx resulting in the course of the rise in the systemic blood pressure. That this explanation is correct may readily be gathered from a study of the general character of the curve. While the rise develops very shortly after the onset of the stimulation, a longer latent period cannot rightly be expected in this case, because the general blood pressure has been registered in these experiments in the femoral artery, i.e., very close to the seat of the primary vasoconstriction. The remaining extent of the curve, however, exhibits a perfect parallelism with the height of the blood pressure.

About fifteen seconds after the beginning of the stimulation, the oncometer tracing of the right kidney exhibits a sudden decline which, in some cases, merely attains the level of the record previous to the stimulation and, in others, reaches much below this line. The left kidney retains its small volume during this period, or if a relaxation of its blood vessels has already set in, a secondary decline may result. As this belated decrease in the volume of the kidneys occurs synchronously with the second elevation in the curve of the systemic blood pressure, it must be ascribed to the action of the adrenalin which has been liberated by the left adrenal body in consequence of the excitation of its secretory nerve. Obviously, the severity of this indirect vasoconstriction of the renal blood vessels must be in complete agreement with the secretory activity of the gland. Late in the course of an experiment of this kind, and especially if the stimulations have been repeated too frequently, the decrease in the volume of the right organ becomes less abrupt and may eventually disappear altogether. It need scarcely be mentioned that the second summit may also be destroyed at any time by temporarily obstructing the suprarenal vein. The volume curve of the right kidney pursues under this condition a course parallel to the record of the systemic blood pressure.

In figure 2 the changes are depicted which result in consequence of the excitation of the right splanchnic nerve. We observe first of all the almost instantaneous decrease in the volume of the right kidney occasioned by the direct vasoconstrictor action of this nerve, and secondly, the initial increase in the volume of the left kidney which, however, is soon followed by a diminution. In this case, naturally, the right suprarenal gland is responsible for the outpour of adrenalin. It is again to be noted that the right splanchnic nerve does not exercise a direct control over the state of the vasomotor mechanism of the left kidney.

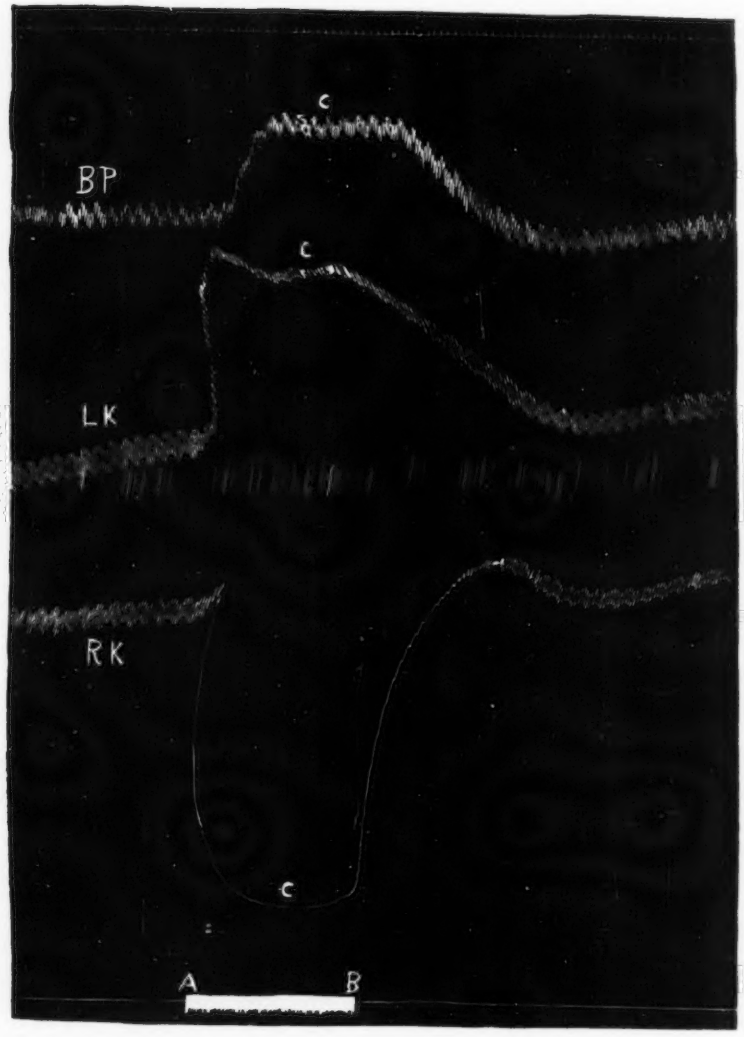

Fig. 2. Stimulation of the right splanchnic nerve (15 cm., 24 seconds)

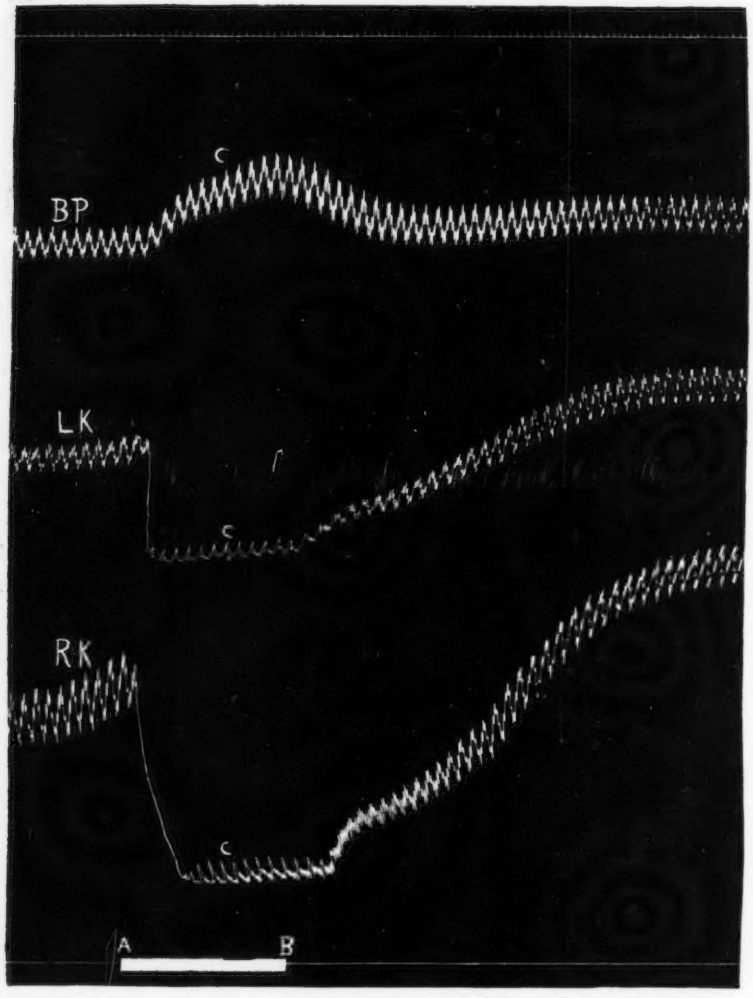

Fig. 3. Stimulation of both splanchnic nerves (13 cm., 25 seconds)

Figure 3 is intended to serve as an example of those reactions which were obtained by the simultaneous stimulation of the left and right splanchnic nerves. The oncometric tracings now show almost immediate decreases in accordance with the bilateral constriction of the renal blood vessels. In these cases the subsequent discharge by the two adrenal bodies generally failed to augment the primary effect in a very noticeable manner, but it is possible to render the secondary reaction more conspicuous by lessening the amplitude of the primary. This end can readily be attained by decreasing the duration and strength of the stimulation; in fact, it is possible to adjust the latter in such a manner that perfectly parallel curves may be obtained from the two kidneys.

These experiments, therefore, uphold my previous contention that the innervation of the kidneys is unilateral and enable me moreover to explain the peculiar changes in the blood supply of these organs which I obtained on contralateral stimulation of the splanchnic nerves. The initial increase in the flow I have attributed correctly to the rise in the general blood pressure, because as the kidney on the opposite side is not directly affected by the stimulation, its vascularity must be subject to the changes in the arterial driving force. The subsequent decrease in the blood supply for which at that time I could offer no explanation, now finds its true solution in the secondary constriction of the renal blood vessels by the adrenalin.

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SOME OF THE GENERAL PHYSIOLOGICAL PROPERTIES OF DIAPHRAGM MUSCLE AS COMPARED WITH CERTAIN OTHER MAMMALIAN MUSCLES

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CONTENTS

1. Introduction 446
2. The relation of oxygen 449
3. The method of stimulation 454
4. The degree of irritability 455
5. The single contraction 456
6. The working power 457
7. Summation of stimuli 462
8. Rhythmicity 463
9. The power of resistance to deleterious influences 467
   a. Fatigue 467
   b. Death of body 467
   c. Curare 468
   d. Trichiniasis 469
   e. Heat and humidity 469
   f. Fasting 470
10. Summary 471

1. INTRODUCTION

The diaphragm, because of its unique position in the mammalian body, its unique structure, and its unique action, has always been an object of interest. Haller (1), writing in 1733 his "De musculis diaphragmatis dissertatio anatomica," mentions some fifty writers, beginning with Plato and Aristotle, who had set forth their views, as the result of speculation, or observation, or experimentation, concerning the action and use of this peculiar muscle. To Fabricius (2) has been ascribed the first recognition—in 1603—of the true action of the diaphragm in respiration, but Haller, with his clear-sighted vision, contributed materially to an understanding of its function, and since Haller's time the literature concerning it has been considerable. But with

all that has been said upon its gross anatomy and its specific physiology one searches almost in vain for enlightenment regarding its histological structure, its chemistry, and the general physiological properties of its muscular tissue. It seems strange, indeed, that more thought has not been given to its general physiology, for this topic, even on slight consideration, appears promising. In importance to the individual the diaphragm ranks highest of all skeletal muscles: although its bilateral paralysis, whether from trauma or disease of the nervous system, is not rare, the continuance of life in such a condition is difficult, if not impossible. Moreover, while most skeletal muscles in the living body contract with varying degrees of intensity and at irregular intervals between which occur long periods of rest, the diaphragm from the time of birth to that of death performs day and night a continual succession of brief contractions of a fairly regular rhythm and fairly uniform in extent, alternating with brief intervals of rest. Thus this muscle, together with other respiratory muscles, holds a unique position among skeletal muscles and suggests a crude analogy with the heart. Like the heart too, the diaphragm performs during the lifetime of the individual an incredibly huge amount of work, probably more than any other skeletal muscle.

In view of these facts it might be expected that a careful study of this important muscle would reveal physical and chemical peculiarities which would distinguish it from other muscles. Such a study was planned by the senior author several years ago, and since then work upon it has been carried on from time to time, as opportunity has permitted. The results of the physical portion of the research, as here presented, justify the predictions, for it is shown that the diaphragm does possess distinctive general physiological properties.

Preliminary experiments were made with the diaphragms of the cat, the rabbit and the guinea pig, but that of the cat proved most satisfactory and was chosen for detailed study. Its behavior under the various experimental conditions has been contrasted with that of certain muscles of the leg, such as the extensor longus digitorum, the sartorius, and the soleus, and at times the muscular tissue of the heart. The extensor and the sartorius were chosen as typical pale muscles, the soleus as the type of red muscles. The diaphragm appears intermediate between these two in color. We shall see that in physiological properties color is a feature of limited significance.

We have used for our experiments only a certain part of the diaphragm, namely, a strip extending along both sides of its anterior

median line from the bone and cartilage of the ensiform process to the central tendon. This is the strip which in the rabbit is unusually well isolated and has been widely used in recording the contractions of the muscle in respiration. In the cat it is not so much separated from the rest of the muscle, but by observing the direction of its fibers one can readily cut it out with a minimum of injury. Its average dimensions are 50 mm. in length, and from 10 to 20 mm. in breadth. It appears to consist of long parallel fibers. That the fibers are, in fact, long and extend practically from one end of the strip to the other, is indicated by the results of stimulating the muscle electrically in a manner suggested by Kühne's unipolar method. The secondary coil of an inductorium is provided with two electrodes: one formed by a metal plate, on which lies a curarized strip of the diaphragm, and the other consisting of a fine needle which is carefully brought to touch the muscle. With the interrupter of the inductorium in vibration and with an electrical current that is not too strong, the plate serves as an indifferent, the needle as an active, electrode. Under such circumstances it can be seen that the muscle contracts over an area twenty to thirty times as long as it is broad. Furthermore, after maceration for twenty-four hours in nitric acid, the strip can be torn into delicate threads running its entire length, and under the microscope these can be seen to consist of a dozen or more long muscle fibers. The sartorius of the cat is a large muscle, consisting of a thick lateral and a thin mesal paler portion. We have used only the latter. Its fibers are very long, but whether they extend actually from end to end of the muscle, we cannot say. In the extensor longus digitorum and the soleus, of which muscles the whole substance has been used for study, the fibers extend, not longitudinally, but diagonally, from an aponeurotic extension of one tendon to a similar extension of the other in the case of the extensor, and to the long tibial insertion in that of the soleus.

No one appears yet to have made an exhaustive study of the histological structure of the diaphragm and its histological relations to other muscles. Schiefferdecker (3), using human and canine diaphragms, has most nearly approached this, but his results, while intrinsically of importance, do not appear to be specifically related to our physiological facts. In both man and dog he finds scattered large muscle fibers of a more or less circular cross-section, surrounded by small fibers which appear in section polygonal and often with sharp corners. He argues that in the larger fibers the protoplasm is under a higher tension, although he does not know their specific function. In both the

large and small fibers of the human diaphragm, while most of the nuclei lie just under the surface, a relatively larger number than is usual in other muscles lie more deeply; in the dog's diaphragm almost all the nuclei are superficial. We have examined sections of the several varieties of cat's muscles that have been used in our experiments. No very striking differences have been observed. The sections of the diaphragm have shown considerable differences in the size of cross-sections of individual fibers, but no grouping of large round, surrounded by small polygonal, fibers. The cat's fibers resemble the dog's, however, in the almost exclusively superficial location of the nuclei.

2. THE RELATION OF OXYGEN

Ehrlich (4), in his classic work on the oxygen requirements of the organism, found that after the injection of a solution of indophenol white certain groups of muscles including the diaphragm, besides the heart, the brain, and the kidney, appeared blue owing to the oxidation of the drug, and he pointed out that it is these organs, which are of the most importance to the organism, "die vor allen anderen am wenigsten reductionskräftig, d.h. relativ am besten mit Sauerstoff gesättigt sind." Bonhöffer (5), using a method that had been employed by Bernstein (6) and even before him by Yeo (7) under Kronecker's direction, found that the quickly acting pale muscles of the rabbit, guinea pig and rat reduced oxyhaemoglobin more rapidly than the slowly acting red muscles. Knoblauch (8) too, employing one of Ehrlich's methods, observed in rabbits after death in tetanus resulting from the administration of alizarin blue S, which reduces to alizarin white, that the red muscles, such as the soleus, the semitendinosus and the masseter, still remained red, while the pale muscles were blue—the explanation being found in the fact that the more rapidly fatiguing pale muscles quickly lost their reducing power, which the resistant red muscles still retained. Rehns (9) found that after injecting into mice a soluble salt of paraphenylenediamine the diaphragm oxidized the salt and hence was stained blackish during life, while all other muscles, save those of the eye and the larynx though in lesser degree, required the aid of the atmospheric oxygen to effect the oxidation. Nothing analogous appeared in the rabbit, guinea pig, and rat; nevertheless, Rehns concluded that the diaphragm is peculiar among muscles in possessing a superabundant supply of available oygen. The results of these four men suggest that muscles in relation to oxygen may exhibit two differences: They

may differ not only in their power to reduce oxygen-containing chemical substances, but in the amount of oxygen which they contain.

We have studied the general problem in the four cat's muscles by several methods. In an endeavor to discover any differences in reducing power that might distinguish the muscles we injected strong solutions of alizarin blue S subcutaneously into ten cats and after killing the animals observed the degree of coloration of the various muscles. While the method proved not altogether satisfactory and decisive, owing to uncertainty in the distribution of the substance throughout the body, it afforded some evidence that the diaphragm possesses the greatest power of reduction of all the muscles. We next turned to a simpler method *in vitro*, using oxyhaemoglobin as the indicator, and here we obtained very striking and uniform differences in reducing power. A solution was prepared by mixing 1 part of cat's blood with 99 parts of distilled water. To this was added enough sodium chloride to bring the mixture to an 0.8 per cent solution of the salt, and 7 cc. of this were placed in each of four flat bottles. The animal was killed by decapitation and the four muscles were quickly dissected out. One gram of each was rubbed up in 0.7 grams of powdered glass and placed at once in the blood solution, which was then covered by a layer of olive oil to exclude the air. (When these experiments were performed we were not acquainted with Vernon's work on the solubility of air in fats—Proc. Roy. Soc., B, 1907, lxxix, 366. We have no reasons, however, to believe that the facts which he presents would alter our general results.) The finely pulverized muscle and glass settled to the bottom, and the oxyhaemoglobin of the supernatant solution became progressively reduced from below upward. The specimens were observed with the direct vision spectroscope at frequent intervals and the time was noted at which in each the spectrum of oxyhaemoglobin gave place to that of reduced haemoglobin. In order to insure exactness of measurement observation was confined to the layer of the solution that was in immediate contact with the muscles and the width of which just equalled the length of the slit in the spectroscope. The results of the thirteen experiments performed are given in table 1.

The reducing power of the four muscles is seen to be greatest in the diaphragm and to descend in the order: diaphragm, extensor, sartorius, soleus; the average time required for the last being more than four times that of the first in the series.

The same general result was confirmed by means of extracts of the muscles and methylene blue in experiments which were conducted as

follows: The four muscles were removed as quickly as possible after the death of the animal, and a gram and a half of each was weighed out. Each of these portions was ground in a mortar with 2 grams of glass powder for 10 minutes. The four preparations were placed in 30 cc. of distilled water, and the mixtures were thoroughly stirred and allowed to extract for one hour at room temperature. At the end of this time they were centrifuged for at least 15 minutes, and subsequently, if a deposit had appeared on the surface, the supernatant fluid was filtered. Five cubic centimeters of each of these extracts were added

TABLE 1

Reducing power of muscles, as measured by the number of minutes required to reduce oxyhaemoglobin

NUMBER OF EXPERIMENT	DIAPHRAGM	EXTENSOR	SARTORIUS	SOLEUS
1	19	56	55	372
2	18	16	50	280
3	25	28	31	55
4	24	22	53	144
5	44	21	88	99
6	44	40	45	80
7	52	65	70	246
8	23	37	51	47
9	25	40	42	44
10	48	22	54	117
11	38	41	42	77
12	24	30	58	109
13	27	27	38	138
Average.....	32	34	52	139
Percentage.....	100	106	162	434

to an equal quantity of a weak aqueous solution of methylene blue in a test tube, the mixture was covered with paraffin oil, and the rate of reduction was judged by the disappearance of the blue color, which began at the bottom and progressed upward. Decoloration of most of the solutions was complete in from 1 to 3 hours with most of the muscles, but with the extract of the soleus it required some 2 days. In addition to the test tubes containing the extracts of the four muscles there were always two controls. The first contained a sample of the solution of methylene blue but no muscle extract; it underwent no change of color. The second control contained the dye and the usual quantity of one of the muscle extracts, but the mixture was boiled for a half minute; its

color became slightly lighter immediately upon adding the extract and before boiling, but thereafter there was no change. Seven observations were made with muscles taken from 6 cats. The order in which the several extracts reduced the dye is given in table 2.

It is here seen that, as with oxyhaemoglobin, the diaphragm possesses the greatest, the soleus the least, reducing power; the two pale muscles hold an intermediate position with the sartorius slightly in the lead.

The mechanism of the process of biological reduction is not yet agreed upon. Harris and Creighton (10) have presented data which they interpret as evidence in favor of the existence of a specific reductase in the organs of the animal body. If we accept their interpretation we may say that the diaphragm possesses the most reductase, the soleus

TABLE 2

Reducing power of muscles, as measured by the order in which extracts of the muscles reduce methylene blue

NUMBER OF EXPERIMENT	ORDER OF REDUCTION	
1	Di Sar Ext Sol	
2	Di Sar Ext Sol	
3	Di Ext Sar Sol	Ext. and sar. reduced almost simultaneously
4	Di Sar Ext Sol	
5	Di Sar Sol Ext	
6	Di Ext Sar Sol	Same extract as in Exp. 5. Ext. and sar. reduced simultaneously
7	Di Ext Sar Sol	

the least. But, whatever the mechanism, the facts show that there exist pronounced and constant differences in reducing power in different muscles and that, of all the muscles studied, the cells of the diaphragm possess the greatest power to utilize the oxygen of their environment. In this respect the diaphragm is a superior physiological mechanism.

In an endeavor to learn whether Rehns' conclusion as to the existence of a reserve supply of oxygen in the diaphragm of the mouse holds good for another mammal, we have made fifteen autopsies on cats, after injecting solutions of the hydrochloride of paraphenylenediamine during life into various places—subcutaneously, the carotid artery, the external jugular and femoral veins, the thoracic cavity, the abdominal cavity, and immediately over the site of the three leg muscles that have been studied. The presence of available oxygen at any place

would be indicated by the drug there becoming dark purple or blackish. No injections into the blood vessels resulted in staining of the muscles or other tissues. Injections into the thorax or abdomen stained the muscles at the point of injection and seemed to indicate a selective action toward the drug on the part of the diaphragm, but the results were not clear cut, the decision was left doubtful, and the method was abandoned. A few observations on the results of mixing a solution of paraphenylenediamine with extracts of muscles, prepared in the same manner as in the above experiments with methylene blue, were also indecisive, and we are, therefore, forced to leave unsolved this part of our problem. We may, however, point out that even Rehns was unable to confirm in the rabbit, guinea pig and rat his findings on the mouse, and that thus his generalization as to the diaphragm in

TABLE 3

The order in which extracts of muscles plus hydrogen peroxide oxidize paraphenylenediamine

NUMBER OF EXPERIMENT	ORDER OF OXIDATION	
1	Di Sar Ext Sol	
2	Di Sar Ext Sol	
3	Di Ext Sol Sar	
4	Di Sar Ext Sol	
5	Di Sar Ext Sol	Same extract as in Exp. 4.
6	Sar Sol Di Ext	Sar. and sol. oxidized simultaneously.

comparison with other mammalian muscles is hardly justified. Moreover, the blackening of the muscle with paraphenylenediamine does not make it necessary even in the mouse to assume a greater actual reserve supply of oxygen. The important fact, which we have shown by our experiments on reduction, is the greater capability of the tissue of the diaphragm to extract oxygen from its immediate environment. Our experiments also make it probable that this peculiarity of the tissue is dependent on the existence in it of an enzyme—it may be extracted from the muscle cells by water and it may be destroyed by heat. Such an enzyme might be a reductase or an oxidase—the existence of either could explain the observed facts—or it might be an enzyme with reversible power. But at present we are not warranted in drawing further or more definite conclusions.

We may, however, be permitted to quote here a few observations that we have made which may possibly bear on the obscure subject of

peroxidases. Four or five cubic centimeters of the extract of each muscle were poured into a test tube containing an equal quantity of a saturated solution of paraphenylenediamine. Two cubic centimeters of a 0.6 per cent solution of hydrogen peroxide were added in order to give an excess of oxygen as a peroxide, and the tubes were observed for a darkening of the solution. At the end of 2 or 3 hours the colors were finally compared and the results were recorded. The depth of color indicated the degree of oxidation. Six observations were made with the muscles of 5 animals, and the results are given in table 3.

As with reduction, so here the diaphragm ranks first, the soleus last, with the extensor and sartorius between, the latter again leading the extensor.

3. THE METHOD OF STIMULATION

Our experiments in which stimulation was employed have been performed on excised muscles. The animals were killed by decapitation, which occurred instantaneously and painlessly. The muscles were then carefully removed, suspended in moist chambers at room temperature, and attached to light straw levers arranged to record the contractions isotonically. This procedure required usually from 5 to 15 minutes. Thus treated, the muscles of the cat remain irritable and in excellent experimental condition for a considerable time. We can highly recommend such preparations, especially the diaphragm strips, for the general study of muscle phenomena, for demonstration, and for students' use; in various features they are superior to frogs' muscles. The stimuli which we have used were induction currents, usually single break shocks from a Krüger inductorium with the secondary coil placed at 10 cm. In the earliest experiments a single Grove cell was used in the primary circuit. Later this cell was replaced by a small Edison storage battery, and the current in the primary circuit was kept uniformly at 0.7 ampere. The stimuli were maximal in all cases, except where otherwise stated. The electrodes were attached to the two ends of the muscles. In many of our experiments two muscles were used simultaneously for comparison; at such times they were placed in series in the secondary circuit, and the one induction shock stimulated both. The weights lifted were, in most of our experiments, alike for the various muscles, the weight that was usually attached to the lever near its axis being 100 grams, which was equivalent to 10 grams actually lifted by the muscle. In certain experiments weights proportional to the cross-sections of the muscles were employed,

the calculations being made according to the method of Funaoka (11), namely:

$$\frac{\text{Weight of muscle}}{\text{Specific gravity } (=1.04)} = \text{Volume} \qquad \frac{\text{Volume}}{\text{Length}} = \text{Average cross-section}$$

Computed in this way from 13 specimens of each of the muscles the average cross-sections in square centimeters were as follows: Diaphragm, 0.188; sartorius, 0.192; extensor, 0.275, soleus, 0.349. It was found convenient to use these figures as standard measurements in some of our calculations to be presented later.

4. THE DEGREE OF IRRITABILITY

The relative irritability of the several muscles was measured by determining the threshold of stimulation with the single break induction shock. Only a single muscle from each animal was used and this was

TABLE 4

Irritability of excised muscles as measured by the distance in millimeters of the secondary coil with minimal stimulus from the single break induction shock

	EXTENSOR	SARTORIUS	DIAPHRAGM	SOLEUS
	286	393	313	258
	275	358	424	258
	573	481	357	477
	476	295	314	271
	446	425	368	336
Average	411	390	355	320
Percentage	100	95	86	78

removed, attached to the recording lever, weighted with a single gram and tested, with the greatest possible speed, so as to insure the least possible diminution of irritability. The average time which elapsed between the death of the animal and the determination of the threshold was 7 minutes. Five experiments were performed with each of the four varieties of muscle and the results are given in table 4.

Although the variations in irritability of each variety of muscle here shown are considerable, the average differences between the different varieties are probably sufficient to be significant. The extensor proved to be the most irritable and the other muscles follow in the order:

sartorius, diaphragm, soleus. Thus, in the degree of irritability to single induction shocks, the diaphragm lies between the pale muscles on the one hand and the red muscle on the other.

5. THE SINGLE CONTRACTION

The single contractions of the four varieties of muscle differ in certain physical characteristics, as is well shown in figure 1. The diaphragm contracts very quickly to its maximum, and frequently lifts its load to a greater height than do any of the other muscles. The peak of its curve is rather sharp, relaxation beginning promptly. For one third or one half of its course relaxation is quick; it then slows markedly, and

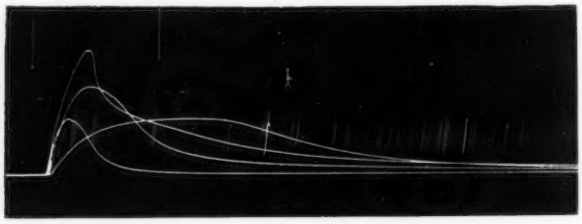

Fig. 1. Curves of the single contraction of four excised muscles of the cat, stimulated by maximal break shocks. The highest curve is that of the diaphragm, the next in height that of the sartorius; the curve of the extensor longus digitorum is low with quick contraction and relaxation, that of the soleus low with slow contraction and relaxation.

from this point onward the return of the lever to the abscissa is very gradual. The sartorius exhibits an equally quick contraction. In the figure its curve is next in height to that of the diaphragm; sometimes it lifts the weight to the greatest height of all the muscles. Relaxation begins slowly and the whole upper half of the curve is much broader than that of the diaphragm; in its latter half the relaxation is still slower but, in general, similar to that of the diaphragm. The curve of the extensor is much like that of the sartorius, but it is on a much smaller scale, so that both contraction and relaxation are completed earlier than with any of the other muscles. The soleus behaves like a typical red muscle; the height of its curve is about equal to that of the extensor, but its contraction is very slow, reaching its maximum only when all the other muscles are well along in their relaxation. Its

relaxation too is prolonged, although in the final stages less so than the relaxation of the diaphragm.

Besides these physical differences in the character of the single contraction there are differences in the duration of the latent periods. These we have measured in 6 specimens of each variety of muscle. Only a single muscle was taken from each animal, a weight of only 1 gram was employed, and records of from 4 to 8 single contractions with maximal stimulation were quickly made on a rapid drum. An average period of less than 13 minutes elapsed between the death of the animal and the completion of the records. Thirty-five measurements of the latent period were made with the diaphragm and 40 with each of the other muscles. The averages are given in table 5.

TABLE 5

Latent periods of excised muscles in seconds

	EXTENSOR	DIAPHRAGM	SARTORIUS	SOLEUS
	0.00492	0.00861	0.00720	0.00925
	0.00509	0.00561	0.01000	0.01144
	0.00428	0.00738	0.01047	0.00810
	0.00537	0.00794	0.00990	0.00895
	0.00418	0.00734	0.00795	0.00969
	0.00459	0.00780	0.00666	0.00915
Average.....	0.00474	0.00745	0.00869	0.00943
Percentage.....	100	157	183	199

The striking feature here is the fact that the quickly contracting pale extensor exhibits the shortest latent period and the sluggish red soleus the longest, the duration of the two being as 1:2. The stimulated diaphragm gets into action before both the sartorius and the soleus, but not as quickly as the extensor.

6. THE WORKING POWER

The diaphragm is far superior to the other muscles in the power to do work. This has been demonstrated in two ways: first, by comparing the total amount of work which the several muscles are capable of doing before becoming exhausted; and, secondly, by comparing the absolute powers of the muscles.

In comparing the total amount of work of the muscles we followed the method outlined on page 454. The excised muscles were stimulated

usually at the rate of 28 shocks in the minute, the contractions were recorded on a slow drum as a series of successive vertical lines, and the experiments were continued until the muscles were exhausted. Two muscles from the same animal were usually studied simultaneously. The data here reported give the duration of the working period and the total amount of work that was performed. The amount of work was computed from a measurement by a Coradi planimeter of the total area that was covered in the graphic record by the series of contraction curves. The terminal portion of such an experiment is usually long drawn out, since the muscles, after accomplishing their chief task, continue to respond to the stimuli by minute twitches for a considerable time. The amount of work done in this terminal phase is slight, and measurement of its area in the graphic curve was found to introduce considerable error. It was possible, however, to measure down to a point where the recorded curves just ceased to be 1 mm. in height, with an error of not more than 2 per cent. In the interests of accuracy, therefore, each experiment has been regarded as ceasing at such point, both as regards working period and total work accomplished.

Figure 2 shows characteristic records for the four muscles, the later portions of the records being given only in sections. In initial extent of contraction the diaphragm frequently led, and the other muscles usually followed in the order: sartorius, extensor, soleus, the height of the initial curves of the two latter not differing greatly. The sartorius was usually alone in making a few introductory contractions, rapidly diminishing in height; the diaphragm occasionally performed such contractions. The diaphragm and the sartorius usually exhibited a treppe, which was the more pronounced in the diaphragm. A treppe was rarely present in the extensor, and was absent in the soleus. After the maximum of contraction was reached all the muscles exhibited the usual gradual course of fatigue on to exhaustion, although they differed greatly in the duration of their activity. Table 6 gives precise measurements of the duration of the working power and the total amount of work that was performed by the several muscles. These figures are averages of 14 specimens of the diaphragm, 13 of the extensor, 15 of the sartorius, and 14 of the soleus. The records were made in an investigation, by the senior author and Dr. E. L. Scott, of the working power of muscles when the animals were subjected to different atmospheric conditions. The animals were here kept for a period of 6 hours in a chamber constantly supplied with an abundance of fresh air of a fairly uniform temperature, averaging 20.5°C., and

of a relative humidity of 52 per cent. This was a combination of conditions that were especially favorable to the organism. Directly after removal from the chamber the cats were killed and the muscles

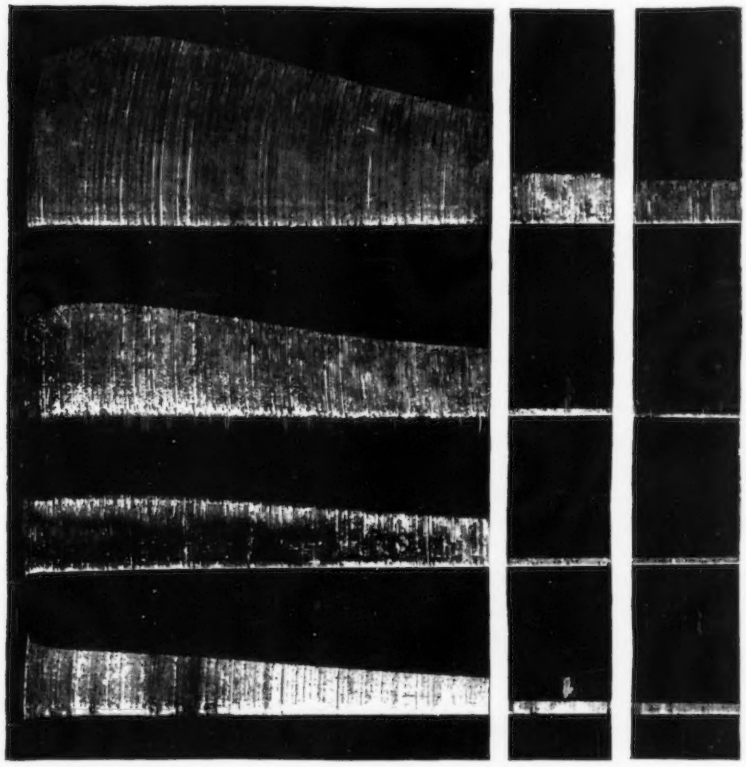

Fig. 2. Curves of series of contractions of four excised muscles of the cat, stimulated by maximal break shocks 28 times per minute and lifting equal loads. From above downward the respective curves are from the diaphragm, the sartorius, the extensor longus digitorum, and the soleus. The selected records belong to corresponding periods of time.

were studied. The details of the experiments will be published elsewhere. In these experiments the actual areas of the cross-sections of the several muscles were not measured, but if we employ the standard

cross-sections given on page 455 and calculate the total work accomplished per square centimeter of cross-section, we obtain the figures given in table 7.

These tables show that, considered as a machine to do work, the diaphragm is easily the leader of all the other muscles—it works longer and it does more work before becoming exhausted. The long-fibered sartorius can accomplish only about half as much; while the compact short-fibered extensor and soleus perform for each unit of cross-section only one-seventh to one-eighth of the diaphragm's achievement. The latter, in fact, both in the small strip used and in unit of cross-section,

TABLE 6

Average working period and total work of excised muscles before exhaustion; animals subjected to favorable atmospheric conditions

	DIAPHRAGM	SARTORIUS	SOLEUS	EXTENSOR
Working period:				
Minutes	148	121	84	72
Percentage	100	82	57	49
Total work:				
Gram-millimeters	147,957	76,599	31,593	30,224
Percentage	100	52	21	20

TABLE 7

Total work of excised muscles per square centimeter of cross-section before exhaustion; animals subjected to favorable atmospheric conditions

	DIAPHRAGM	SARTORIUS	EXTENSOR	SOLEUS
Gram-millimeters	787,005	398,953	109,905	90,524
Percentage	100	51	14	12

performs much more work than all the other muscles together. In considering this marked difference it should be mentioned that, as we shall see later, the diaphragm survives all the other muscles after death. But this is probably only a minor factor in its power to accomplish much work before exhaustion. Undoubtedly of more importance are its greater ability to utilize oxygen, its greater content in glycogen, which has been determined by Lee, Scott and Colvin and will be discussed by them in a subsequent paper, and perhaps other factors.

In determining the absolute power of the several muscles we employed the original method of Weber, that is, we determined the maximum load that the afterloaded muscles were just incapable of lifting. We then used the figures thus obtained, together with the standard figures for cross-sections, in computing the absolute power per square centimeter of cross-section. Table 8 shows the results of such determinations in 10 specimens of each muscle.

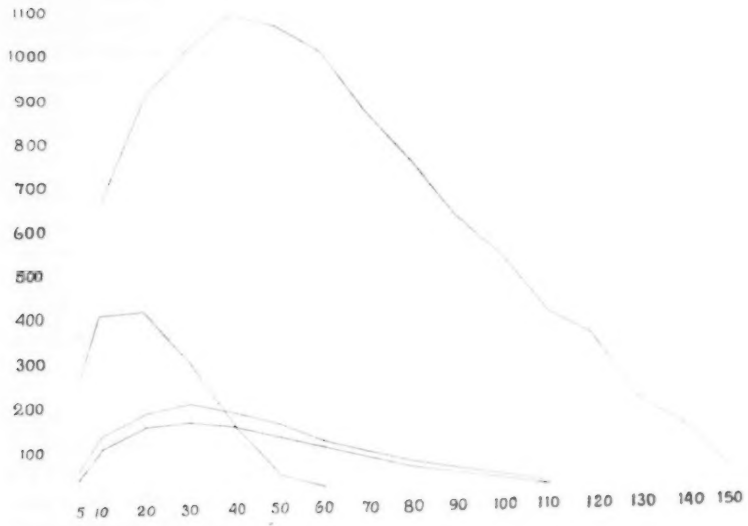

Fig. 3. Composite curves of work of excised muscles of the cat, each curve representing the average of 5 muscles. The order of decreasing height is: diaphragm, sartorius, extensor longus digitorum, and soleus. Abscissa indicates successive grams lifted; ordinates, work done in gram-millimeters per square centimeter of cross-section.

In making the determinations of absolute power it is not a question of survival, for the tests were made quickly after the excision of the muscles; it is simply a question of lifting loads, of doing work. Here the diaphragm is seen again to be far in the lead. It is followed in order by the extensor and soleus, possessed respectively of but three-quarters and one-half of the power of the diaphragm. Last comes the sartorius, relatively weak, with an absolute power of less than one-third.

If the curves of work be plotted for the several increments of load

beginning with the lightest and proceeding gradually to the heaviest possible and calculating the observed data in terms of unit of cross-sectional area, we have a result as shown in figure 3, which is a composite curve representing the average of 5 observations on each variety of muscle. This reveals, most strikingly of all the various ways of looking at the matter, the supremacy of the diaphragm.

Thus, however viewed, the diaphragm, as a working mechanism, is vastly superior to all the other muscles studied. It lifts a greater load, it is capable of lifting it to a greater height, it continues to work for a longer time, and it performs before it becomes exhausted a much greater amount of labor. All of these powers are greatly to its advantage in the important rôle that it plays in the life of the individual.

TABLE 8

Absolute power of excised muscles, measured in grams per square centimeter of cross-section

	DIAPHRAGM	EXTENSOR	SOLEUS	SARTORIUS
Average	599	458	314	188
Percentage	100	76	52	31

7. SUMMATION OF STIMULI

In the course of many of our earlier experiments on stimulation it became obvious that the four varieties of muscle differed as to their power of summating stimuli. This was finally tested, with the assistance of Mr. C. A. Worth, by the following method. A single muscle was removed from an animal as soon as possible after death, and was prepared for a graphic record. The threshold of irritability for single induction shocks was determined, and the records of a few supraminimal contractions with augmenting stimuli were made. Then the stimulus was increased suddenly to a maximum and a series of contractions was recorded, usually 50 in number at a convenient rate of 28 in the minute. Immediately thereafter the stimuli were reduced to the former supraminimal intensity, and a few contractions were recorded analogous to the first series, but in the reverse order—that is, with stimuli progressively diminishing in intensity back to the threshold. The location of the threshold and the intensity of the contractions following each grade of supraminimal stimulation indicated the degree of the irritability of the muscle at the beginning and at the end of the

test; the maximal stimuli were employed to augment the irritability, if such were possible, and thus make manifest the power of summation, if such were present. Any augmentation of irritability might readily be explained by the action of metabolites in small quantity, as suggested by the senior author (12) for the treppe. Summation was manifested either by an increase in the extent of supraminimal contraction, or by a lowering of the threshold, or by both together. We have tested in this way 11 diaphragms and 6 of each of the other varieties of muscle. With the diaphragm some degree of summation was always capable of demonstration; with the other muscles it was either absent or showed only very feebly.

The power of a muscle to summate stimuli, that is, the power rapidly to augment responsive contractions upon a slight expenditure of stimulus, is doubtless of advantage to the muscle, and here the diaphragm seems to be superior to the other muscles studied.

8. RHYTHMICITY

The tendency of skeletal muscular tissue to respond by visible twitches, more or less rhythmical in character, to tetanic stimuli much more rapid in rate, or to constant stimuli, such as are afforded by a galvanic current or by solutions of inorganic salts, has received much attention from investigators. One of us (A. E. G. 13) has made, in the sartorius muscle of the frog, a special study of this property and its relation to various ions. In our earlier experiments it appeared to be highly developed in the excised diaphragm, as was readily demonstrated by subjecting the usual strip of the muscle, arranged to record its contractions, to a weak faradic current of from 40 to 200 shocks in the second. As the interrupter in the primary circuit we have used the hammer of the inductorium vibrating at the rate of 48 times in the second, and tuning forks of 20, 50, and 100 v.d. provided with the usual electric platinum-contact device. The responsive contractions were then found to occur usually at a rate of from 1 to 4 in the second, although always somewhat irregular in both frequency and extent, the rate increasing with increasing strength of the stimulating current. If the current were very weak these were the only visible signs of stimulation; but if it were slightly strengthened the muscle might fall into a tetanus, with the twitches superimposed as waves upon the smooth tetanic curve. With still further increase of stimulus the response became still more complex and irregular in both rate and intensity,

and a single muscle was often found to manifest all degrees of response from the simple to the complex type. All the three other skeletal muscles that we have studied were found to exhibit the same phenomenon, although, as shown by the extent, the frequency, and the regularity, of the individual twitches, the diaphragm led all. The order in

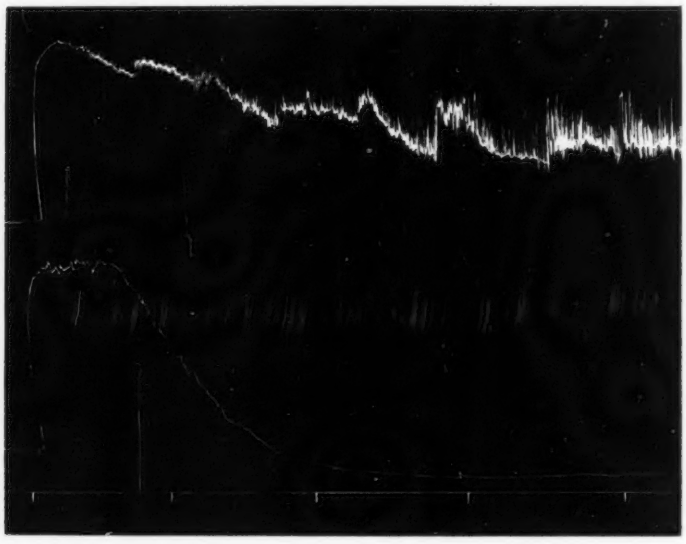

Fig. 4. Curves of contraction of two excised muscles of the cat (upper, diaphragm; lower, sartorius), produced by immersing the muscles in an aqueous solution of equal parts of $\frac{N}{8}$ sodium chloride and $\frac{N}{8}$ sodium oxalate at 35–40°C. Note the greater tendency of the diaphragm to perform "rhythmic" twitches. Time curve records minutes.

which they were arranged as to the degree of such "rhythmicity" was: diaphragm, extensor, sartorius, soleus, the difference between the extensor and the sartorius, however, being slight.

Similar twitches may be readily demonstrated by immersing the muscles—we have tried the diaphragm, the sartorius and the soleus—in solutions of various electrolytes. We have used for this purpose sodium oxalate, sodium tartrate, sodium carbonate, sodium sulphate, and potassium chloride, usually in one-eighth normal solutions and at a temperature of 35–40°C. A very satisfactory solution consists of equal parts of $\frac{N}{8}$ sodium chloride and $\frac{N}{8}$ sodium oxalate. Figure 4

shows a record obtained with this solution. With all of these substances the diaphragm usually exhibits twitches more numerous and of greater extent than do the other muscles.

In analysing this "rhythmic" tendency as it is demonstrated by the faradic current the first step, naturally, is to exclude any rhythm arising from the stimulating apparatus. For this purpose a method analogous to that of Samojloff (14) has been found convenient. It consists in hanging two strips of the same muscle in series and passing through them the same current, in the same direction, at the same time, and with the same area of contact at the electrodes. Synchronous twitches may then be looked upon as conditioned possibly by an irregularity in the stimulating current. If, on the other hand, the twitches are not synchronous, they may be regarded as conditioned primarily by factors residing in the muscles. We have used this method with the diaphragm only. Certain complications detract somewhat from the clearness and definiteness of the results. Thus, the contractions frequently may differ in height so that in one of the strips they may be barely or not at all evident. As the stimulation is continued, however, the apparently quiescent muscle may begin to show more and more marked contractions while the previously active strip becomes quiescent. Our tests have shown that such variations are not due to changes in the gross relative irritabilities of the two strips. Now the more irritable and now the less irritable preparation may exhibit the more pronounced twitches. But, notwithstanding such differences, most of the twitches appear to be synchronous in the two strips and hence presumably are of instrumental origin.

Samojloff has laid stress upon the imperfections for physiological use of the common methods of interrupting the primary current. Our experience has demonstrated that the presence of a spark gap is fatal to uniformity of successive shocks. Even the introduction of a condenser across such gap in the inductorium, while diminishing the frequency and intensity of the twitches, has failed to eliminate them altogether. Where, therefore, uniformity of successive stimuli is desired, as is especially the case with submaximal stimuli, some device other than the ordinary interrupter with metallic contacts must be found. We have, hence, sought for a different method of stimulation and have found a statisfactory apparatus in a simple alternating current generator consisting of an armature revolving in a field of permanent magnets. For the use of such an apparatus we are indebted to Drs. R. H. Cunningham and H. B. Williams. A photographic record of its

alternations of potential, made by means of a string galvanometer, shows a series, not of true sine waves, but of waves almost uniform in amplitude and form. The apparatus was set for a speed of 25 cycles, or 50 shocks, in the second and was introduced into the primary circuit of our inductorium. We then obtained with all of our muscles perfectly smooth tetanic curves with no sign of twitches, whatever the intensity of the stimulating current. This experiment seems to prove beyond a doubt that most of the previous "rhythmic" responses to the faradic current originated in quantitative irregularities of the shocks supplied by the interrupter.

But this is not the whole story, for the following striking facts still remain: (1) The diaphragm is much more prone to exhibit such twitches than are the other muscles; (2) there is occasional asynchronism when both of two diaphragm strips are giving well-marked contractions; and (3) the twitches are frequently present in one strip and the other alternately. Furthermore, if it is wholly a question of the irregularities of the stimuli, how are we to explain the similar "rhythmicity" and the similar greater proneness of the diaphragm to it in the presence of electrolytes? Is it possibly a question of differences of polarization with faradic stimuli and differences of permeability with chemical stimuli? Moreover, if we accept Lucas's view that the individual fibers of striated muscle obey the "all-or-none law" and thus reach with our submaximal stimuli only a portion of the fibers in the whole muscle, are we to suppose that now certain groups of fibers are active, and now others, and that differences in the irritability of different groups of fibers play a part in the phenomenon?

A further step in the analysis of the "rhythmicity" might consist in the exclusion of the nerve. This we believe that we have done through the rapid death of the nerve in our mammalian preparations. The phrenic ceases to respond to stimuli within a very few minutes after death and we have no reason to believe that either the intramuscular filaments of the nerve or the motor end-plates continue irritable for a much longer period. Nevertheless, we have been interested in testing the "rhythmic" tendency of muscles after the administration of curare to the animals and then killing them after paralysis has set in. In such cases the responses to both faradic and chemical stimuli are markedly weakened, although they are not eliminated entirely. The curarized muscles are much more prone to pass directly into unbroken tetanic contractions. Has the curare affected the receptive substance of Langley in such a manner as to make the muscle less susceptible to irregularities in the stimuli?

We thus see that our consideration of the "rhythmicity" of the various muscles, so far as we have carried our experiments at the present time, raises more questions than it answers, and we are not now prepared to propose even an hypothesis with any degree of confidence to account for this great susceptibility of the diaphragm to respond to the ordinary faradic and chemical stimuli by "rhythmic" twitches.

9. THE POWER OF RESISTANCE TO DELETERIOUS INFLUENCES

So far we have considered chiefly those general physiological properties that the several muscles may make use of in their ordinary activities. We have now to turn to their behavior under certain unusual circumstances and especially those conditions that may act unfavorably to the muscles.

a. Fatigue. We may recall here, first, the comparative powers of resistance to extreme fatigue that the muscles show, a power that is measured by the amount of time that elapses before the contracting muscle becomes exhausted and by the total amount of work that it is capable of doing—a power that is far more marked in the diaphragm than in the other muscles.

b. Death of body. A similar difference exists in resistance to death after excision from the body. Here we have made a series of observations with the assistance of Mr. C. A. Worth. The four varieties of muscle excised from the same animal and placed within moist chambers, were weighted with only 2 grams each and were tested at intervals of fifteen minutes as to their power to respond to the stimulus of the usual maximal induction shocks. The duration of survival was measured by the time that elapsed between the moment of decapitation of the animal and the moment of the last visible response of the muscle to stimulation. Table 9 gives the results of ten observations. Compare these with the observations formerly reported by the senior author (15) on the tibialis anticus and the soleus.

This table illustrates the great variations in the power of survival that are exhibited by individual muscles of the same kind. Notwithstanding this the pronounced lead of the diaphragm over the other muscles is obvious. Its long period of survival after death, namely, 9 hours and 44 minutes, is half again as long as that of the red soleus and more than twice as long as that of the pale extensor and sartorius—in other words, the diaphragm is extremely hardy.

c. Curare. It is often said that the diaphragm is the last muscle of the body to succumb to the action of curare. So far as we have been able to learn, this statement is based on Boehm's (16) experiment of 1895. We have made our own observations on several cats and are able to affirm that the statement is true. Our cats were etherized and tracheotomized for the further administration of ether, and the brachial and sciatic nerves were freed from their surrounding tissues. A few cubic centimeters of a 2.5 per cent solution of curare in physiological salt solution were then injected into either the jugular or the femoral vein, a second dose being given later. The brachial and sciatic nerves were stimulated at intervals with a faradic current and the resulting

TABLE 9

Duration of survival of excised muscles after death, expressed in hours and minutes

NUMBER OF EXPERIMENT	DIAPHRAGM	SOLEUS	EXTENSOR	SARTORIUS
1	16: 45	12: 25	6: 25	5: 40
2	6: 55	5: 10	3: 10	3: 55
3	3: 55	4: 40	2: 40	2: 40
4	11: 45	11: 00	5: 00	3: 15
5	4: 36	6: 51	3: 11	7: 21
6	10: 00	6: 20	6: 20	2: 50
7	8: 15	2: 15	2: 15	8: 15
8	12: 00		4: 15	5: 00
9	14: 43	6: 58	3: 43	2: 18
10	8: 30	5: 45	6: 15	2: 00
Average	9: 44	6: 49	4: 19	4: 19
Percentage	100	69	44	44

contractions of the leg muscles were observed. When these muscles ceased to respond to supramaximal indirect stimuli, even though the heart was still beating and maintaining the circulation of the blood, the phrenic nerves were exposed and stimulated by the same strong current and were found still capable of causing the diaphragm to contract. It is hardly necessary to mention that careful precautions were taken against an escape of current. At this stage of the experiment the diaphragm had usually ceased its natural contractions, or they were so weak and irregular as to be incapable of maintaining a sufficient respiration. Meyer and Gottlieb (17) state that "by administering the proper dose [of curare], it is possible to keep a rabbit alive for hours with all its muscles paralyzed except the diaphragm." It is evident that,

whatever the mechanism—and the mechanism is not entirely evident—the diaphragm is more resistant to the action of curare than are the other skeletal muscles. In this connection it may be mentioned that Calmette (18) states that after poisoning by the bite of the cobra respiration becomes difficult and assumes the diaphragmatic type. This fact should be more fully investigated and its exact significance should be determined.

d. Trichiniasis. It is a known fact that in trichiniasis the diaphragm, together with the intercostal muscles and those of the jaw, the tongue and the eye, is infested with the parasites to a far greater extent than are other skeletal muscles. Rehns (9) correlates this fact with

TABLE 10

Average working period and total work of excised muscles; animals subjected to unfavorable atmospheric conditions

	DIAPHRAGM	SARTORIUS	EXTENSOR
Working period:			
Minutes	142	88	54
Percentage	100	62	38
Percentage loss in working period when compared with table 6	4	27	25
Total work:			
Gram-millimeters	117,317	52,965	23,624
Percentage	100	45	20
Gram-millimeters per square centimeter of cross-section	624,027	275,859	85,905
Percentage	100	44	14
Percentage loss in work when compared with table 6 or 7	21	31	22

the greater supply of oxygen which he assumes to be present in the diaphragm. Stäubli (19) ascribes, without proof, the superabundance of trichinae to a greater blood supply of the muscles in question. Here is further opportunity for investigation.

e. Heat and humidity. In connection with the investigation made in coöperation with Scott and referred to on page 458, we have studied the results of exposing cats to unfavorable atmospheric conditions, and report in table 10 our average figures of the working period and the total work performed. Before the muscles were studied the animals were confined for a period of 6 hours in a well-ventilated chamber, the air of which possessed an average temperature of 32.8°C. and an

average humidity of 90 per cent, that is, the atmospheric condition was analogous to that of one of the hot and humid summer days in an American city and would have been markedly uncomfortable to a human being. The computations in unit of cross-sectional area were made with the aid of the standard figures given on page 455. Observations were made upon 12 diaphragms, 13 sartorii, and 13 extensors; the soleus was not here studied.

The figures of this table will be appreciated only when they are compared with the corresponding data recorded for animals that had been kept under favorable atmospheric conditions, as presented in tables 6 and 7. It will then be observed that the high temperature and the high humidity to which the animals of the present series were subjected before being tested exercised a deleterious influence on the organism, which is expressed in a diminished working period and a diminished total amount of work performed by the muscles. This phenomenon will be discussed in detail and in relation to other data in a report by Lee and Scott. What especially interests us now is the relative effects of the harmful conditions on the three muscles. The working period of the extensor is reduced by 25 per cent and that of the sartorius by slightly more, 27 per cent, while the diaphragm suffers only a 4 per cent reduction. As to working power the sartorius has lost nearly one-third, the extensor and the diaphragm only one-fifth, with the advantage slightly in favor of the latter muscle. Thus, of all the muscles, the diaphragm is least affected by the unfavorable atmospheric conditions.

f. Fasting. In connection with an investigation of some of the physiological effects of inanition, which is being carried on by the senior author together with Morgulis and Scott, the effects of fasting on the diaphragms and the extensors of 10 cats have been studied. The animals were allowed water but no food; the average duration of the fasting period was 15 days; and the average loss in bodily weight was 33 per cent. The details of the work will be published elsewhere, but the average results are given in table 11.

We see here that, as might be expected, there is a great falling-off both in the duration of the working period of the two muscles and in the total amount of work performed. The effect of inanition may be best appreciated when the results are compared with those of the muscles of tables 6 and 7, which were in a good nutritive condition. As regards the working period the diaphragm is again affected less than the extensor, the percentage decrease of the total time being 30 and 40 respectively. As regards the total amount of work that the muscles

are capable of performing the result is different: the fasting diaphragm has lost 44 per cent of its working power, the fasting extensor only 16 per cent. The respiratory muscle thus suffers to a much greater extent than does the leg muscle. We are not prepared to offer an explanation of this exceptional fact, but we cannot refrain from suspecting that it is associated in some way with the diaphragm's greater activity. The observations on fasting are not yet completed.

TABLE 11

Effect of inanition on the average working period and the total work of excised muscles

	DIAPHRAGM	EXTENSOR
Working period:		
Actual, in minutes	104	43
Percentage	100	41
Percentage loss in working period when compared with table 6	30	40
Total work:		
Actual in gram-millimeters	82,888	25,295
Percentage	100	31
Actual in gram-millimeters per square centimeter of cross-section	440,894	91,982
Percentage	100	21
Percentage loss in total work when compared with table 6 or 7	44	16

10. SUMMARY.

This paper is devoted to a comparative study of several of the general physiological properties of four skeletal muscles of the cat—the diaphragm, the extensor longus digitorum, the sartorius, and the soleus. The general results of the study may be summarized in table 12. Here, after the designation of each physiological property, the degree in which it has been found present in the several muscles is given. The order is from the greatest to the least in all items, except the length of the latent period, in which this order is reversed.

The most common order in which the several muscles may be arranged as to the quantitative development of the various general physiological properties is: diaphragm, sartorius, extensor, soleus. The properties appear least pronounced in the red soleus; and next in the two pale muscles, with the sartorius slightly in the lead. As to most of the properties the diaphragm stands by itself in the lead of all the others.

Its tissue possesses the greatest reducing power, in other words, the greatest power to remove oxygen from its environment, and this power is probably dependent on the existence of an enzyme; its content in peroxidase is greatest; the irritability of the excised diaphragm to single induction shocks, while surpassed in degree at first by both the extensor and the sartorius, survives long after all the other muscles have died; in the brevity of its latent period the excised diaphragm is surpassed by the extensor only; when actively stimulated and made to do work

TABLE 12

Order in which muscles exhibit physiological properties

Reducing power with oxyhaemoglobin	Di Ext Sar Sol
Reducing power with methylene blue	Di Sar Ext Sol
Content of peroxidase	Di Sar Ext Sol
Irritability to single induction shocks	Ext Sar Di Sol
Length of latent period	Ext Di Sar Sol
Working period in cool dry air	Di Sar Sol Ext
Total work per square centimeter of cross-section in cool dry air	Di Sar Ext Sol
Absolute power	Di Ext Sol Sar
Power to summate stimuli	Di Other muscles
Tendency to "rhythmicity"	Di Ext Sar Sol
Resistance to fatigue	Di Sar Sol Ext
Duration of survival after death	Di Sol [Ext Sar]
Resistance to curare	Di Other muscles
Tendency to trichiniasis	Di Other muscles
Resistance to heat and humidity: working period	Di Sar Ext
Resistance to heat and humidity: total work per square centimeter of cross-section	Di Sar Ext
Resistance to inanition: working period	Di Ext
Resistance to inanition: total work per square centimeter of cross-section	Ext Di

the excised diaphragm will work for a much longer period and accomplish far more than the other muscles—even more than all together—before becoming exhausted; it is superior in absolute power and in tendency to summate stimuli; it exhibits a greater tendency than do the other muscles to respond to faradic and chemical stimuli by twitches, more or less rhythmical in character; its greater resistance to fatigue is exhibited in its longer working period and its greater work accomplished before becoming exhausted; it, with possibly some other respiratory muscles, is the last skeletal muscle of the body to submit to the paralysing action of curare; other investigators have pointed out its greater tendency than other parts of the body to harbor trichinae

—a peculiarity that is not yet explained, but may possibly be associated with the greater power of the diaphragm to utilize oxygen; when the body is subjected to high heat and high humidity all the muscles (the soleus not having been studied) are affected deleteriously, which is manifested in a diminution of the working period and the total work that can be accomplished before exhaustion sets in, but the diaphragm is affected far less than the other muscles; by extreme inanition the total working period of the excised diaphragm is shortened far less than that of the extensor, although the total work that can be performed by the former is diminished to a greater degree—a fact that may possibly be associated with the greater activity of the diaphragm.

Most of these facts indicate that the diaphragm possesses much more efficient muscular tissue than do the other muscles—in other words, it is a superior physiological mechanism. This is exactly what might be expected, when the unique and superior rôle of the diaphragm among skeletal muscles is considered. Here seems to be a striking instance of physiological adaptation to physiological requirements.

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SOME OF THE CHEMICAL PROPERTIES OF CERTAIN MAMMALIAN MUSCLES

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In the course of the investigation of the general physiological characteristics of certain muscles of the cat, which has been carried on by the senior author together with Guenther and Meleney (1), it proved desirable to know in some detail the chemical constitution of the same muscles and their chemical changes under various experimental procedures. The present paper presents the results of the first portion of this research and consists of a partial chemical analysis of the muscles in question, which are the diaphragm, the extensor longus digitorum, the sartorius, and the soleus. The extensor and the sartorius are pale red in color, and possess in general the physiological properties of pale muscles; the soleus is deep red with the general physiological behavior of dark muscles; while the diaphragm, intensely red in color, cannot be classed physiologically with either of these two classes, but seems in many respects to stand by itself as a superior physiological mechanism. It leads all the other muscles in most of the general physiological properties that have been studied. It is superior in the power of survival after death, in reducing power, in content of peroxidase, in power to work long and to accomplish much before becoming exhausted, in absolute power, in tendency to summate stimuli and to respond to faradic and chemical stimuli by more or less rhythmical twitches, and in resistance to fatigue, to curare, to the depressing action of high heat and humidity, and to inanition. In most of these features the soleus stands at the other end of the series, while the extensor and sartorius occupy an intermediate position, with the sartorius slightly in the lead.

It is obviously desirable to know whether any correlation exists between the physical behavior and the chemical properties of the muscles in question, and a search for such correlation is the main purpose of the present studies. We can hardly pretend yet to have made much advance in this direction. Our present analyses, indeed, should be re-

garded merely as constituting a reconnaissance, a preliminary survey of a field which appears to be large and not altogether unpromising.

So far the work has been confined to a determination of the chemical elements other than carbon, hydrogen, and oxygen, and of glycogen. In spite of the fact that a distribution analysis would increase the experimental error by the introduction of additional technical procedures and the reduction of the absolute amounts of substances determined, it was thought that the greater physiological significance of the results would warrant the use of this method, which, therefore, we have followed. Since some points have thus been revealed that must have been overlooked by the more direct method, we believe that the results have justified our course. This is especially true in regard to the distribution of the sulphur.

The animals were killed by swift and painless decapitation. The muscles were quickly removed and cleaned so far as possible of external fat, fascia and tendons. From the diaphragm the pleural and peritoneal coverings and the tendinous center were removed. In every case samples of the four muscles were taken from each cat used. The size of the samples (about 30 grams of fresh tissue from 12 to 15 muscles) was determined partly by convenience in extraction and partly by the fact that the material was to a large extent a by-product from other experiments and was collected as opportunity offered. This resulted in the samples being so small that great accuracy in the determination of the inorganic salts could not be expected. Although, in general, the results for the inorganic salts have not been used in our correlation of the chemical and physical properties of the muscles, the analyses were made in the hope that the results would at least point the direction for further and more detailed work; and we believe that this consideration warrants their publication.

The method of separation is that described by Koch (2) and his collaborators. For its details the reader is referred to the original papers. Briefly, the material was collected in a sufficient quantity of redistilled alcohol to make the final concentration of alcohol between 85 and 90 per cent. It was then extracted alternately with alcohol and ether. This operation was carried out in an apparatus so arranged that the actual extraction took place at a temperature but little below that of the boiling solvent.

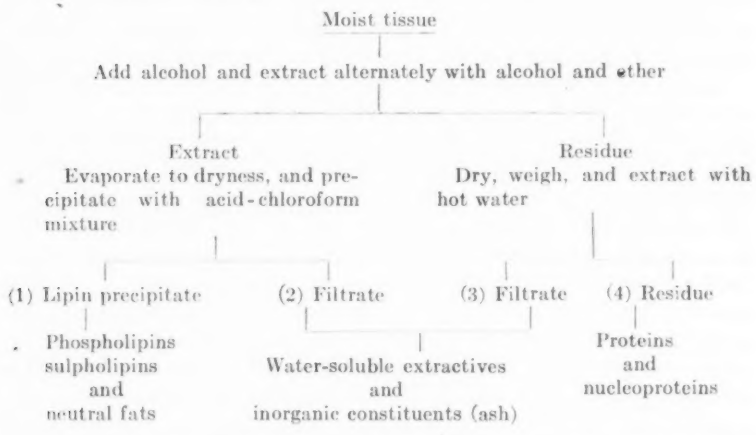
In this manner the lipins and a certain amount of the water-soluble extractives were separated from the proteins and the remainder of the water extractives. The lipins were then precipitated from the extrac-

tives by acidulated chloroform, and the lipin phosphorus and sulphur were determined. The extractive fraction was dried and ashed in hydrochloric and nitric acids, and the iron, magnesium, calcium, potassium, sodium, phosphorus, and sulphur were determined.

The alcohol-ether insoluble portion was extracted repeatedly with boiling water, the ash of the extractives was obtained in the same manner as above, and the same determinations were made.

The nitrogen, phosphorus and sulphur of the protein fraction were determined.

The fractionation may be formulated as follows:



In the present paper it is not thought necessary to describe the detail of the methods used in the determination of the several constituents, further than to say that the sulphur and phosphorus of fractions 1 and 4 were determined as described by Koch, and the determinations in fractions 2 and 3 were made by the official methods of the Association of Official Agricultural Chemists (3). In the calculations of fractions 2 and 3 corrections were made for the material not removed from the lipin and the protein fractions. In the former case this was done by the method of aliquot parts; in the latter a portion of the protein residue was ashed and the correction was calculated from the ash recovered. In both cases the corrections were small, of the order of 2 per cent.

While in some cases, especially of the inorganic salts, the percentage of variation between the findings in parallel determinations is larger than is desired, it should be remembered that our parallel determi-

nations were made upon actually different samples, collected at different times, rather than on different portions of a homogeneous sample prepared from a single animal. In this way the variations between samples are added to the technical error. Since, with the one exception discussed below, we have not considered in our interpretation of

TABLE 1

Water, solids, and elementary constituents of muscles in grams per 100 grams of total solids. The figures are the averages found for each of the four muscles studied, together with the averages for those of the series. The figures found by Katz for cat's muscle are given for comparison.

CONSTITUENTS		DIAPHRAGM	EXTENSOR	SARTORIUS	SOLEUS	AVERAGES OF THE SERIES	KATZ'S AVERAGES
Water		73.26	75.15	73.36	75.42	74.14	75.136
Solids		26.74	24.85	26.64	24.58	25.86	24.863
Lipins: Fraction 1	Total weight	11.73	7.69	11.52	14.13	10.86	
	Phosphorus	0.1673	0.1803	0.2128	0.1704	0.1835	0.1166
	Sulphur	0.0314	0.0424	0.0495	0.0718	0.0469	
Inorganic salts: Fractions 2 and 3	Iron	0.0308	0.0235	0.0337	0.0393	0.0309	0.0372
	Calcium	0.0356	0.0280	0.0615	0.0474	0.0401	0.0341
	Magnesium	0.0729	0.0570	0.0773	0.0508	0.0642	0.1152
	Potassium	1.5154	1.6412	1.2601	1.6352	1.5251	1.5576
	Sodium	0.8751	0.5108	0.5474	0.7229	0.6536	0.2932
	Phosphorus	0.5042	0.6236	0.5786	0.5380	0.5620	0.6192
	Sulphur	0.1872	0.3101	0.2674	0.3251	0.2670	
	Chlorine						0.2257
Proteins and nucleoproteins: Fraction 4	Total weight	69.1	73.4	69.9	68.4	70.5	
	Nitrogen	11.159	11.539	11.119	11.214	11.275	
	Phosphorus	0.1119	0.1449	0.1785	0.0863	0.1267	0.0748
	Sulphur	0.5220	0.5286	0.4872	0.4864	0.5088	
Total phosphorus		0.7834	0.9488	0.9699	0.7947	0.8722	0.8106
Total sulphur		0.7406	0.8811	0.8041	0.8833	0.8227	0.8748

results those which varied greatly in this way we have not felt warranted in encumbering this paper with the extended tables that would be necessary to show all the figures. However, the averages for most of the constituents agree rather closely with those of Katz (4), who also studied the muscles of the cat as well as of other animals.

Tables 1, 2, and 3 show the average results of the determinations of water, solids, and elementary constituents, and table 4 the more detailed results for sodium and potassium. In table 1 the results have been calculated in grams per 100 grams of total solids; in table 2 in grams per 100 grams of fresh tissue; and in table 3 there are given the gram-atoms of the various elements (gram-molecules in the case of

TABLE 2

Elementary constituents of muscles in grams per 100 grams of fresh tissue. The figures are the averages found for each of the four muscles studied, together with the averages for those of the series. The figures found by Katz for cat's muscle are given for comparison.

CONSTITUENTS		DIAPHRAGM	EXTENSOR	SARTORIUS	SOLEUS	AVERAGES OF THE SERIES	KATZ'S AVERAGES
Lipins: Fraction 1	Total weight...	3.137	1.911	3.069	3.47	2.81	
	Phosphorus....	0.0447	0.0448	0.0567	0.0419	0.0475	
	Sulphur.....	0.0084	0.0105	0.0132	0.0176	0.0121	
Inorganic salts: Fractions 2 and 3	Iron.....	0.0082	0.0058	0.0090	0.0097	0.0080	0.0093
	Calcium.....	0.0095	0.0070	0.0164	0.0117	0.0104	0.0085
	Magnesium....	0.0194	0.0142	0.0206	0.0125	0.0166	0.0286
	Potassium.....	0.4052	0.4078	0.3357	0.4019	0.3944	0.3083
	Sodium.....	0.2340	0.1269	0.1458	0.1787	0.1690	0.0729
	Phosphorus....	0.1348	0.1550	0.1541	0.1322	0.1453	0.1539
	Sulphur.....	0.0501	0.0771	0.0712	0.0799	0.0690	
	Chlorine.....						0.5662
Proteins and nucleoproteins: Fraction 4	Total weight...	18.48	18.24	18.621	16.813	18.22	
	Nitrogen.....	2.9839	2.8675	2.962	2.7563	2.9157	
	Phosphorus....	0.0299	0.0360	0.0476	0.0212	0.0328	0.1859
	Sulphur.....	0.1396	0.1314	0.1298	0.1193	0.1316	
Total phosphorus		0.2095	0.2358	0.2584	0.1953	0.2256	0.2016
Total sulphur		0.1980	0.2190	0.2142	0.2171	0.2128	0.2188

water) occurring in 100 grams of fresh tissue. The figures published are the averages of four analyses in the case of the diaphragm, the extensor, and the sartorius, except that only two determinations were made of the inorganic salts of the sartorius. The analysis of only two samples of the soleus was attempted. The averages for the entire series were obtained by adding the amounts of the several elements obtained in the different analyses and dividing the sum by the total

number of determinations made. In the last column of tables 1 and 2 Katz's figures are given for comparison.

Our figures for sodium are markedly higher than Katz's, being rather more than twice those which he gives for the cat and well above his figures for any animal except the swine and the haddock. It is probable that a certain amount of sodium was extracted from the glass of

TABLE 3

Water and elementary constituents of muscles. The water is expressed in mols, the other constituents in gram-atoms, per 100 grams of fresh tissue. The figures are the averages found for each of the four muscles studied, together with the averages for those of the series.

CONSTITUENTS		DIAPHRAGM	EXTENSOR	SARTORIUS	SOLEUS	AVERAGES OF THE SERIES
Water		4.0665	4.1714	4.0720	4.1864	4.1153
Lipins: Fraction 1	Phosphorus	0.00144	0.00144	0.00183	0.00135	0.00153
	Sulphur	0.00026	0.00033	0.00041	0.00055	0.00038
Inorganic salts: Fractions 2 and 3	Iron	0.00015	0.00010	0.00016	0.00017	0.00014
	Calcium	0.00024	0.00017	0.00041	0.00029	0.00026
	Magnesium	0.00080	0.00058	0.00085	0.00051	0.00068
	Potassium	0.01036	0.01043	0.00859	0.01031	0.01009
	Sodium	0.01017	0.00552	0.00634	0.00773	0.00735
	Phosphorus	0.00434	0.00050	0.00497	0.00426	0.00468
	Sulphur	0.00156	0.00240	0.00222	0.00249	0.00215
Proteins and nucleoproteins: Fraction 4	Nitrogen	0.21192	0.20467	0.21145	0.19674	0.20818
	Phosphorus	0.00096	0.00104	0.00153	0.00068	0.00106
	Sulphur	0.00435	0.00410	0.00405	0.00373	0.00410
Total phosphorus		0.00675	0.00760	0.00832	0.00566	0.00727
Total sulphur		0.00618	0.00683	0.00668	0.00677	0.00663

the apparatus, and at first we were inclined to think that this was the whole explanation of the large amounts. But it will be noted that our figures for potassium are not very different from those of Katz for cat's muscle. Now, by reference to table 4, it will be seen that with the exception of experiment 12 with the extensor, the potassium-sodium ratio is very nearly a constant for any one kind of muscle; and this is so, re-

gardless of considerable variations in the actual amounts of the elements present. This fact causes us to believe that a possible error from glass is a minor factor in our results, and leads us to point out the possibility that each kind of muscle may have a characteristic potassium-sodium ratio. What the significance of such a specific ratio is, we are not at present prepared to say. Further work in which special attention is paid to the determination of the alkalies is necessary. It

TABLE 4

Sodium and potassium in muscles

MUSCLES	NUMBER OF EXPERIMENTS	GRAMS PER 100 GRAMS OF TOTAL SOLIDS			GRAMS PER 100 GRAMS OF FRESH TISSUE		
		Potassium	Sodium	K/Na	Potassium	Sodium	K/Na
Diaphragm	1	1.3667	0.8417	1.613	0.3660	0.2254	1.624
	4	1.4635	?	?	0.3867	?	?
	9	1.3560	0.8054	1.684	0.3668	0.2179	1.684
	13	1.8755	0.9783	1.917	0.6996	0.2614	1.917
	Average	1.5154	0.8751	1.732	0.4052	0.2340	1.731
Extensor	2	1.4476	0.4852	2.983	0.3518	0.1179	2.984
	5	?	0.5199	?	?	0.1320	?
	8	1.6547	0.6021	2.748	0.4125	0.1501	2.748
	12	1.8214	0.4369	4.169	0.4517	0.1083	4.169
	Average	1.6412	0.5108	3.567	0.4078	0.1269	3.214
Sartorius	7	1.5654	0.6374	2.455	0.4072	0.1658	2.456
	11	0.9547	0.4373	2.183	0.2369	0.1085	2.183
	Average	1.2601	0.5474	2.302	0.3357	0.1458	2.302
Soleus	10	1.4483	0.6241	2.312	0.3600	0.1596	2.257
	14	1.8220	0.8217	2.217	0.4448	0.2006	2.217
	Average	1.6352	0.7229	2.262	0.4019	0.1777	2.262
General average		1.5251	0.6536	2.334	0.3944	0.1690	2.334

is, however, perhaps pardonable to mention the fact that Meigs and Ryan (5) report a potassium-sodium ratio for smooth muscle similar to that which we have found for the diaphragm, while in the cross-striated muscle they find relatively less sodium, as we do in the other three muscles.

In table 5 we have tabulated such of our results with the elementary constituents and such relationships, as seem to be especially significant.

TABLE 5

Summary of certain elementary constituents of muscles, together with ratios which seem to be significant

CONSTITUENTS	UNITS	ACTUAL QUANTITIES CALCULATED AS INDICATED IN COLUMN 2				PERCENTAGE VALUES, THE FIGURES FOR THE DIAPHRAGM BEING TAKEN AS 100			
		Diaphragm	Extensor	Sartorius	Soleus	Diaphragm	Extensor	Sartorius	Soleus
Lipin phosphorus	Per cent of total phosphorus	21.33	19.06	21.94	21.45	100	89	103	101
Water soluble phosphorus	Per cent of total phosphorus	64.35	65.73	59.64	67.69	100	102	93	105
Protein phosphorus	Per cent of total phosphorus	14.27	15.27	18.42	10.86	100	107	129	76
Lipin sulphur	Per cent of total sulphur	4.24	4.80	6.16	8.11	100	113	145	191
Water soluble sulphur	Per cent of total sulphur	25.30	35.20	33.24	36.80	100	139	131	145
Protein sulphur	Per cent of total sulphur	70.51	60.06	60.60	55.05	100	85	86	78
Ratio of lipin phosphorus to lipin sulphur (P/S)	Gram-atoms per 100 grams of fresh tissue	5.54	4.36	4.46	2.46	100	79	81	35
Ratio of soluble phosphorus to soluble sulphur (P/S)	Gram-atoms per 100 grams of fresh tissue	2.78	2.08	2.24	1.71	100	75	80	61
Ratio of protein nitrogen to protein sulphur (N/S)	Gram-atoms per 100 grams of fresh tissue	48.71	49.93	52.22	52.73	100	102	107	108
Ratio of alkaline earths to alkalies (Ca + Mg)/(Na + K)	Gram-atoms per 100 grams of fresh tissue	5.07	4.76	8.45	4.44	100	93	167	88
Ratio of potassium to sodium (K/Na)	Gram-atoms per 100 grams of fresh tissue	1.02	1.89	1.36	1.33	100	185	133	131

Koch and Koch (6) find in their work upon rats' brains that, as the tissue becomes older and, therefore, presumably metabolizes less actively, there is an increase in the concentration of colloidal sulphur and phosphorus. Correlated with this we should expect to find less lipin and protein sulphur and phosphorus in those muscles whose physiological properties are the most marked. This is not wholly the case, however, for while the lipin sulphur increases in a ratio that is approximately inverse to that of most of the physiological properties—that is, the diaphragm contains the least, the soleus the most, and the extensor and the sartorius an intermediate amount—the lipin phosphorus, when considered by itself varies without apparent order. But, if one obtains the ratios between lipin phosphorus and lipin sulphur, he is struck by the fact that they stand in even closer relationship to the physiological properties than does the sulphur by itself, although in this case the ratio is direct. Thus it seems that, the more active muscles contain actually less sulpholipin than those less active, while there is in the lipin fraction of the former relatively more phosphorus, when compared with the sulphur, than there is in the latter. A study of the figures published by Koch and Koch reveals the same decrease in the P/S ratio as the tissue becomes older, though they do not seem to have called attention to this relationship. Similar ratios are present, though somewhat less markedly, in the case of the soluble phosphorus and soluble sulphur. This relationship might perhaps be more striking if separate determinations of the neutral and inorganic sulphur had been made.

Our figures for protein sulphur vary directly with both the reducing and the working powers of the three groups of muscles, rather than inversely, as would have been the case had they harmonized with the theory of Koch and Koch. This, however, is very suggestive in the light of the possibility that the cysteine and cystine of the protein molecule are closely related to cellular respiration, as is suggested by Mathews (7). The striking difference between our ratios and those found by Koch and Koch leads one to wonder whether the mechanism of respiration in muscular and in nervous tissues is not as fundamentally different as are their physiological activities.

In view of the very interesting work recently reported by Clowes (8) we are giving the ratios between the alkaline earths and the alkalies (table 5, line 10). So far, however, we have been unable to correlate these ratios with any of the specific physiological properties.

Our figures for glycogen are given in table 6. In the separation of the glycogen from the muscle Pflüger's (9) method was followed, with only

the modifications made necessary by the small samples used. The central tendon of the diaphragm was rejected, the sample for analysis consisting only of the muscular tissue together with its pleural and peritoneal coverings. In the case of the paired muscles the muscles from both sides were used. Here superficial fascia and tendinous matter were removed, so that the sample represented only muscular tissue so far as was possible. The average weights of the samples were as follows: diaphragm 5.5 grams; extensor 5.2 grams; sartorius 4.2 grams; soleus 5.6 grams. To reduce destruction of the glycogen the muscles were placed in the hot alkali as quickly as possible after removal from the animal and digestion on the steam bath was continued within a few minutes. However, to neutralize any destruction of glycogen that might have taken place during the removal, the muscles were taken out in the definite order: diaphragm, extensor, soleus, sartorius, for the first half of the series, while the order was reversed for the last half of the series. The final determination of sugar was made by Munson and Walker's (10) method; but the small quantities of sugar obtained in some cases required an experimental extension of their table.

TABLE 6

Glycogen in muscles in grams per 100 grams of fresh tissue

NUMBER OF EXPERIMENTS	DIAPHRAGM	EXTENSOR	SARTORIUS	SOLEUS	AVERAGES	REMARKS
1	0.409	0.283	0.431	0.331	0.363	The muscles in experiments 1–5 were removed in the order: diaphragm, extensor, soleus, sartorius; those in the remaining experiments in the reverse order.
2	0.318	0.138	0.081	0.153	0.175	
3	0.469	0.340	0.194	0.244	0.312	
4	0.202	0.287	0.141	0.076	0.177	
5	0.282	0.259	0.126	0.105	0.192	
6	0.179	0.189	0.087	0.031	0.122	
7	0.182	0.045	0.062	0.093	0.095	
8	0.232	0.095	0.088	0.090	0.126	
9	0.245	0.172	0.119	0.102	0.160	
Average.....	0.280	0.201	0.148	0.136	0.191	
Percentage...	100	72	53	48		

As might have been expected with such a shifting substance, the quantities of glycogen in the different specimens vary considerably. The ratios of the averages, however—diaphragm 100, extensor 72, sar-

torius 53, soleus 48—are sufficiently distinct to be of importance. The two extremes are here again exhibited by the diaphragm and the soleus, the former containing more than twice the amount of glycogen found in the latter. The two pale muscles take an intermediate position with the extensor in the lead. These differences are best interpreted in the light of the following facts.

The reciprocals of Lee, Guenther and Meleney's figures for the reducing power of the muscles, as measured by the percentage number of minutes required to reduce oxyhaemoglobin, are, respectively, diaphragm 100, extensor 94, sartorius 62, soleus 23. These figures and those for the glycogen content, though not actually the same, are alike in forming a descending series with the muscles in the same order. That this general parallelism is not a thing of chance is well shown by comparing the order in which the muscles occur in the several analyses, as shown in table 6.

It is natural to seek correlation also in working power. If we consider this feature, as measured by the total work done by the several excised muscles per square centimeter of cross-section, we find Lee, Guenther and Meleney's figures to be: diaphragm 100, sartorius 51, extensor 14, soleus 12. Here again the diaphragm comes first, the soleus last, and the two pale muscles between, although these two have changed places with one another. This exception to the order is probably of minor significance.

The main feature of our comparison here is that, as regards the amount of glycogen contained in the muscles, their capacity to remove oxygen from their environment, and their capacity to perform work, the diaphragm is always in the lead, the soleus is always last, and the two pale muscles occupy an intermediate position. We cannot help believing that these facts are indicative of a physiological correlation between the three features.

SUMMARY

The present paper contains the results of a determination of the chemical elements other than carbon, hydrogen, and oxygen, and of the glycogen occurring in four muscles of the cat, namely: the diaphragm, the extensor longus digitorum, the sartorius, and the soleus; together with an endeavor to correlate those results with certain of the physiological properties of the same muscles. We have found that:

1. The quantity of lipin sulphur and of water-soluble sulphur is least in the diaphragm, greatest in the soleus, and intermediate in the exten-

sor and the sartorius; that is, the quantity of non-protein sulphur varies inversely to the order in which most of the general physiological properties of the muscles are expressed.

2. The ratios between the lipin sulphur and the lipin phosphorus and between the water-soluble sulphur and the water-soluble phosphorus vary directly as most of the general physiological properties of the muscles.

3. The protein sulphur varies directly as most of the general physiological properties of the muscles, and is possibly to be correlated with muscular respiration.

4. The glycogen content is greatest in the diaphragm, least in the soleus, and intermediate in the extensor and the sartorius. It thus varies directly as most of the general physiological properties of the muscles, and is to be especially correlated with their reducing power and their working power.

5. For each muscle there seems to be a specific ratio between the potassium and the sodium.

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THE ACTION OF TEMPERATURE AND HUMIDITY ON THE WORKING POWER OF MUSCLES AND ON THE SUGAR OF THE BLOOD

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It is a fact of common experience that a human being in a hot and humid atmosphere feels a disinclination to perform muscular work. If we accept the testimony of various observers, this disinclination is accompanied by actual diminution of working power. Thus, Boycott (1) says that his observations on miners working in hot moist air lead him "to conclude that their power of doing work under these circumstances is quite small." Pembrey's (2) "results show definitely that a man is much less efficient in a warm moist atmosphere." Cadman (3), in his work of mine inspection, says that at 35°C., wet-bulb reading, "work becomes impossible." And others testify to the same effect. There are lacking, however, exact data on which to base these inferences, and, even if they be true, it is not clear whether the impairment of the power to do work lies in the central nervous system, or in the muscles, or in both. It has, indeed, been known since the work of Gad and Heymans (4) in 1890 that the excised muscles of frogs become more rapidly fatigued when warmed, and Patrizi (5) demonstrated in 1893 that human muscles when heated by localized hot baths are subject to early fatigue and exhaustion—and these results may have a bearing on this general topic. The internal conditions of labor under extreme conditions of temperature and humidity have been summarized as follows (6):

> When an individual is subjected to an atmosphere that is charged with an excessively high temperature and high humidity, his bodily temperature is raised, his working power becomes limited, and there is an early oncoming of fatigue. In addition to the normal fatigue substances there are present other substances, products of an abnormal metabolism, perhaps of increased protein disintegration, which likewise act as fatigue substances. Both the normal and the pathological fatigue substances act toxically to diminish the activity of the tissues, and such

fatiguing action is rendered greater by reason of the abnormally high internal temperature that is present.

In addition to these conditions there are circulatory changes, a drafting of the blood away from the brain and the muscles to the skin, which may aid in the decrease of working power.

Perhaps the effects of extreme atmospheric conditions are different in kind from those of milder conditions, for preliminary reports of the investigations of the New York State Commission on Ventilation (7) appear to show that in an atmosphere of 30°C. (86°F.) and 80 per cent relative humidity there is a disinclination but not an inability on the part of human beings to perform as much muscular work as in a cooler dryer air.

It is evident that analysis of the subject has not yet gone far enough and that the desired data can best be obtained through experiments on animals. It was with a wish to obtain some of these data that the observations here reported were made. In connection with other work we had perfected methods for studying the working power of muscles and for determining the content of sugar in the blood, and we therefore studied these two topics here—not, however, with the preformed idea of showing any necessary relation between them.

Our plan, first, was to compare the effects on these two physiological phenomena of the exposure of animals, on the one hand, to a fairly comfortable atmosphere and, on the other, to an uncomfortably hot and humid one, such as would be afforded by one of the extreme days of a New York summer. This plan was carried out. Later we completed an additional series using an intermediate temperature and humidity.

We used cats as objects of the experiments and subjected them to the desired atmospheric conditions within a box the ventilation of which was controlled. This box was 46 cm. long, 36 cm. wide, and 35 cm. high; its walls were of galvanized iron, and it contained a wooden floor. A cover, clamped on tightly, closed it at the top. An inlet and an outlet tube, each 14 mm. in diameter, at opposite ends of the box, allowed free passage of abundant air, which was drawn through by a suction pump worked by an electric motor and attached to the outlet tube. This ventilation box was set within a larger box, 66 x 56 x 51 cm. in size, which contained water, and thus the air chamber was surrounded on its four sides and bottom by a water jacket, 10 cm. thick. This water was kept at a desired temperature, which varied with the demands of the individual experiment. The course of the air before entering the ventilation box was circuitous and as follows: By the action of the suc-

tion pump it was taken from the air of the room and passed first into a Williams gas wash-bottle, where it was humidified by being bubbled through water kept at a desired temperature. From this bottle it passed through a lead tube which made eight turns outside the ventilation box within the water jacket, and then entered the box through the inlet tube near the bottom of one end. The outlet tube left the box near the top of the opposite end; from here the outgoing air entered a large glass bottle, which was introduced to protect the pump from excessive moisture, and then passed on to the suction pump, where it was expelled. The cover of the ventilation box contained an observation window and two openings cased with tubing, in which were fixed a dry-bulb and a wet-bulb thermometer. The bulbs of these thermometers projected well into the ventilation box, and the wet bulb with its wick dipping into a small reservoir of water was placed immediately in front of the outlet tube, so that the current of outgoing air swept constantly over the bulb. From the readings of the dry- and wet-bulb instruments the relative percentage of humidity was determined. By carefully controlling the temperature of the water in the water jacket and of that in the Williams bottle, by the use of Bunsen burners or ice, and by the addition of sodium chloride to the water of the wash-bottle in extreme cases where the desired degree of dryness of the air was otherwise difficult to obtain, it was found comparatively easy to control, within the limits desired, both the temperature and the humidity of the air that was supplied to the box. In each experiment a cat was confined within the box for a period of six hours, and records were made every fifteen minutes of the temperature of the air within and of its relative humidity.

At the end of the period of confinement, which was passed usually without excitement and often in a state of repose, the animal was taken quickly from the chamber and killed by swift and painless decapitation. The blood as it flowed from the vessels of the neck was caught in a weighed beaker containing 25 cc. of a 0.5 per cent solution of ammonium oxalate, to prevent coagulation, and was used for the determination of its content of sugar. The muscles that were desired, usually two in number, were excised, and tested for their working power.

The effects of three atmospheric conditions were studied, namely: a comfortable condition, in which the temperature averaged 20.6°C. (69°F.) and the relative humidity 52 per cent; an uncomfortable condition with an average temperature of 32.8°C. (91°F.) and a relative humidity of 90 per cent; and an intermediate condition with an average

temperature of 23.8°C. (74.8°F.) and a relative humidity of 70 per cent. For convenience we will hereafter designate these three conditions briefly as "low," "high," and "intermediate" respectively.

The two physiological phenomena studied will be considered separately.

THE WORKING POWER OF THE MUSCLES

Three muscles were used, all of which are well adapted to the experimental procedures employed. These were the varieties of muscle that were used by Lee, Guenther and Meleney (8) in their study of the comparative physiological properties of various mammalian muscles, and comprised the sternal strip of the diaphragm, the thin flat medial portion of the sartorius, and the extensor longus digitorum. In addition the soleus was used with the comfortable atmospheric condition. Much previous work had shown that all these muscles are very hardy, will survive and respond to stimulation for long periods of time after removal from the body, and may be treated experimentally in much the same manner as the muscles of a cold-blooded animal. From each animal two of the muscles were carefully excised immediately after death, were placed in moist chambers, were attached to isotonic recording levers, were stimulated in series by the same induction shocks, and wrote their contractions as vertical lines, set close together, on the same slowly moving drum. The stimuli were break shocks delivered 28 times per minute, the current of the primary coil being kept at 0.7 ampere, and the secondary coil being placed at 10 cm. The weight attached to each recording lever was 100 grams, one-tenth of which represented the load actually lifted by the muscle. The records were continued until the muscles were practically exhausted. The total work done was computed in the usual manner after measuring the total area of the graphic record by a Coradi planimeter and calculating from this the total height to which the weight was lifted.

The moment of complete exhaustion of a muscle was found difficult to determine: the later contractions of a series differ in extent from one another almost imperceptibly for a considerable period; and even when the graphic curve becomes an apparently unbroken straight line minute twitches of the muscle may still be seen. It was, however, found impossible to measure accurately the area of the graphic record where the successive lifts of the lever were less than 1 mm. in height. To the point where this height ceased the error in successive measurements

TABLE 1

The action of a comfortable, or low, temperature and humidity on muscles

NUMBER OF EXPERIMENT	DATE	SEX	BODY WEIGHT IN KG.	AVERAGE DRY BULB TEMPERATURE IN °C.	AVERAGE HUMIDITY IN PER CENT	DIAPHRAGM		SARTORIUS		EXTENSOR		SOLEUS	
						Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.
1	Apr. 9	F	2.58	20.0	68	148	81,744			77	31,668		
2	Apr. 20	F	2.70	21.2	66	139	164,456			51	36,589		
3	Apr. 22	M	2.45	21.0	54	118	129,067			15	3,817		
4	June 4	F	3.10	21.1	65	171	206,216			104	46,348		
5	June 5	F	3.08	21.3	54	154	112,324			84	25,334		
6	June 10	F	2.70	21.2	59	166	183,072			85	30,437		
7	June 11	M	3.05	21.8	49	120	167,059			55	25,522		
8	June 15	M	3.75	22.1	50	181	146,992	143	63,725				
9	June 16	F	3.80	21.6	49	180	185,841	56	52,543				
10	June 17	F	2.80	21.4	49	150	183,978	36	19,476				
11	June 25	F	2.25	22.0	49	83	112,474	62	39,756				
12	Nov. 21	F	2.30	20.7	51	154	96,008	29	9,950				
13	Nov. 27	F	3.40	21.2	44	167	178,701	25	8,357				
14	Dec. 5		3.10	21.2	51	145	123,463	200	60,858				
15	Feb. 4	F	3.15	19.7	45			197	193,946	65	36,792		
16	Feb. 6	F	3.05	19.8	45			45	19,620	84	36,375		
17	Feb. 9	F	2.25	19.9	46			151	46,111	66	12,624		
18	Feb. 11	M	2.85	20.1	46			203	207,547	124	40,983		
19	Feb. 13	F	3.65	19.9	48			104	46,126	72	38,365		
20	Feb. 18	M	2.75	19.8	51			254	108,387	59	28,053		

21	Mar. 9	M	3.01	19.9	58			137	111,422				
								178	161,160				
22	May 13	M	2.96	19.4	52							194	101,742
												73	12,527
23	May 14	F	3.49	20.0	51							127	40,640
												227	70,116
24	May 17	M	3.35	19.6	50							76	27,172
												36	7,455
25	May 18	F	2.98	18.6	50							26	28,392
												30	26,557
26	May 24	M	2.12	20.3	50							16	9,252
												15	7,085
27	May 25	F	2.90	20.4	52							22	11,794
												103	30,601
28	May 26	F	2.78	20.6	57							161	50,775
												72	17,189
Average			2.94	20.6	52	148	147,957	121	76,599	72	30,224	84	31,593
Percentage						100	100	82	52	49	20	57	21

was not more than 2 per cent. To insure reasonable accuracy, therefore, each experiment was regarded as terminating at this point.

The results of the experiments with the comfortable atmospheric conditions are presented in table 1.

When we examine these data we observe various points of interest. In the first place, with all the muscles, but especially with the sartorius and the soleus, there is a considerable variation both in the duration of the working period and in the amount of work performed by the several specimens. This is a familiar feature to anyone who has studied the work of muscles; it is not peculiar to warm-blooded muscles—the muscles of frogs vary greatly in these respects. It is obvious from the table that the differences have no relation to body weight, sex, or season. So far as we have been able to judge they have no relation to the animals' general nutritive condition. Moreover, similar muscles from opposite sides of the body of a single individual exhibit the differences—as is well shown in experiments 22, 23, 24, 27, and 28, where the two solei were taken from the same cat. The explanation of the variation is not clear. Rather than rule out the extreme cases, as adventitious abnormalities, we have thought it more just to include all in calculating the averages.

In the second place, all the muscles are capable of continuing to work for a remarkably long time after the first stimulus is received, which is good evidence of their hardiness. Here the diaphragm is far ahead of the others, continuing its contractions for an average of nearly 2 and one-half hours, although the extensor, the first to cease, works for an average of 1 hour and 12 minutes. The sartorius and the soleus are intermediate between these two extremes, the former continuing to contract for 2 hours and 1 minute, the latter 1 hour and 24 minutes.

In the third place, the amounts of work performed by the respective muscles are to be noted, and these constitute for our purposes the most interesting feature of all. Lee, Guenther, and Meleney have found that the average cross-sections of the muscles in square centimeters are: diaphragm 0.188, sartorius 0.192, extensor 0.275, and soleus 0.349. It is a striking fact that the muscle that possesses the smallest cross-section, the diaphragm, accomplishes nearly twice as much work as the sartorius and five times as much as either the extensor or the soleus. As a working mechanism the diaphragm is far superior to the other muscles—a fact which has already been discussed by the former authors and need not detain us here.

We turn next to the action of an atmosphere which possesses a dis-

tinctly high temperature and high humidity and is markedly uncomfortable to a human being. Our results are presented in table 2.

TABLE 2

The action of an uncomfortable, or high, temperature and humidity on muscles

NO. OF EXP.	DATE	SEX	BODY WT. IN KG.	AV. DRY-BULB TEMP. IN °C.	AV. HUMIDITY IN PERCENT	DIAPHRAGM		SARTORIUS		EXTENSOR	
						Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.	Duration of work in mins	Work done in gm. mm.
1	Feb. 9	F	3.65	30.7	89	138	89,320			82	24,285
2	Feb. 12	F	1.62	33.1	90	61	42,759			8	2,765
3	Feb. 16	F	3.78	35.0	94	200	150,750			51	25,019
4	Feb. 25	F	2.90	32.9	90	195	110,964			35	15,859
5	Apr. 7	F	3.50	33.7	92	114	111,802			65	31,046
6	June 18	F	2.17	32.5	89	193	166,380	33	18,300		
7	June 19	M	3.85	32.9	89	160	130,330	134	181,385		
8	June 22	F	2.75	32.9	89	106	133,263	32	23,982		
9	June 23	M	3.20	33.2	88	133	170,017	131	32,996		
10	June 24	M	2.50	33.6	89	116	126,112	78	35,274		
11	Dec. 12	M	3.40	32.0	90	130	90,224	13	2,383		
12	Dec. 15	M	2.80	32.4	87			176	74,975	60	26,587
13	Dec. 17	F	3.10	32.6	91			112	50,266	38	19,154
14	Jan. 12	M	3.01	32.2	96	161	85,885			28	13,647
15	Jan. 27	F	3.70	32.6	89			155	117,850	18	6,329
16	Jan. 28	F	3.50	32.8	95			48	38,029	57	18,734
17	Feb. 2	F	2.50	32.8	90			36	13,562	63	22,276
18	Mar. 6	M	3.00	32.7	90			36	14,530		
								161	85,008		
19	Apr. 1	M	3.08	32.5	90					92	48,030
										100	53,376
Average.....			3.05	32.8	90	142	117,317	88	52,965	54	23,624
Percentage.....						100	100	62	45	38	20
Percentage change when compared with table 1.....						−4	−21	−27	−31	−25	−22

Here we have a temperature 12.2° (22°F.) above that of the comfortable condition, and a relative humidity 38 points higher. It is a condition that would be debilitating to human beings, and not without the danger of causing heat-stroke if one were exposed to it for hours and at the same time were obliged to perform physical work. The soleus

was not here studied. The three other muscles again show much variability, in both the duration of work and the total amount of work accomplished; but a computation of the average deviations from the arithmetical average of the total amount of work performed under

TABLE 3

The action of an intermediate temperature and humidity on muscles

NO. OF EXP.	DATE	SEX	BODY WT. IN KG.	AV. DRY-BULB TEMP. IN °C.	AV. HUMIDITY IN PER CENT	DIAPHRAGM		SARTORIUS		EXTENSOR	
						Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.	Duration of work in mins.	Work done in gm. mm.
1	Sept. 26	M	2.72	23.8	73	71	33,304			70	21,434
2	Oct. 3	F	3.00	24.1	71	130	152,606			99	46,316
3	Oct. 10	M	3.80	23.8	72	108	100,336			76	29,082
4	Oct. 15	M	3.30	23.6	69	122	94,604			90	33,257
5	Oct. 17	F	3.30	23.6	70	188	154,431			82	44,739
6	Oct. 22	F	3.00	23.8	70	131	117,192	118	86,879		
7	Oct. 31	F	2.95	23.7	69	178	136,886	47	26,971		
8	Nov. 5	?	2.10	23.6	70	187	116,092	28	7,839		
9	Nov. 7	F	2.25	23.6	70	209	215,734	26	9,089		
10	Nov. 12	F	2.20	23.5	70	205	129,304	181	47,037		
11	Dec. 3	M	3.60	23.6	70	119	87,556			109	42,344
12	Dec. 8	M	2.80	23.7	70	169	153,860	32	10,799		
13	Feb. 20	F	2.09	23.8	70			164	117,279	81	34,976
14	Feb. 23	M	2.04	23.9	70			69	41,022	92	35,698
15	Feb. 25	F	2.05	23.8	70			166	66,028	91	48,071
16	Feb. 27	F	2.07	23.9	70			37	14,588	39	14,051
17	Mar. 4	M	3.00	23.9	70			60	77,223	52	26,930
18	Apr. 6	M	2.96	23.8	70					90	46,973
										91	49,460
19	Apr. 8	F	2.07	23.9	70			161	71,405		
								177	137,038		
Average.....			2.70	23.8	70	151	124,325	97	54,861	82	36,410
Percentage						100	100	70	48	58	32
Percentage change when compared with table 1						+2	−17	−20	−29	+14	+20

the "low" and the "high" conditions reveals a figure lower by about 20 per cent in the latter case. Whether there is a physiological significance in this diminution of variability is not yet clear. The more interesting features are the average changes in the two phys-

iological phenomena. In both of them all the muscles have lost. In the duration of its work the diaphragm has lost 4 per cent, the sartorius 27 per cent, and the extensor 25 per cent; in the total amount of work performed before exhaustion the diaphragm has lost 21 per cent, the sartorius 31 per cent, and the extensor 22 per cent. It is obvious that the high heat and humidity have profoundly affected the muscular tissue so as materially to diminish its effectiveness as a machine.

Let us examine next the action of an atmospheric environment that is intermediate, in respect to the two features studied, between the comfortable and the uncomfortable conditions. The results are presented in table 3.

Here the average temperature was 23.8°C. (74.8°F.) and the average humidity 70 per cent, a combination of the two features which is not ideal, but would not seem markedly unpleasant to a human being or positively bad. With the three muscles the average degree of variability of the two phenomena studied is essentially the same as in the intermediate condition. In the average duration of the working period, when compared with the comfortable condition, the diaphragm is practically unaffected, the sartorious shows a loss of 20 per cent, and the extensor an actual gain of 14 per cent. In the average total amount of work performed both the diaphragm and the sartorius have distinctly lost—17 and 29 per cent respectively—while the extensor is again exceptional in showing a gain of 20 per cent. Thus, on the whole, the effect of exposure of the animal to the intermediate degree of temperature and humidity is a loss in muscular efficiency, the extent of the loss, however, being less than that which results from the more extreme atmospheric condition.

The above results may be surveyed most clearly when they are summarized as in table 4.

It is here seen that as the temperature and the humidity to which the animals are exposed rise, there is a progressive diminution in both the working period of the muscles and the total amount of work which they are capable of performing after excision. The rate at which the working period falls off—low 100, intermediate 97, high 89—is less than that of the work performed—low 100, intermediate 85, high 76—and the latter feature is probably the more significant of the two. It doubtless indicates that metabolic changes are proceeding, which are of such a character that they react deleteriously on the muscle tissue. That the conditions of metabolism are changed is indicated by the results of our determinations of the sugar of the

blood. Without doubt, too, the bodily temperature of our animals was raised when the external temperature and humidity rose—abundant evidence has shown that this occurs in human beings under analogous conditions. But we can not now present specific evidence of changes in metabolism under the conditions of our experiments.

It was pointed out in the introduction to the present paper that a human being in a hot and humid atmosphere feels a disinclination to perform muscular work. Our results seem to indicate that this disinclination rests upon a greater physiological basis than a cerebral condition only, whether this be merely a relative cerebral anaemia or an additional depression of cerebral activity through toxic metabolic products. Besides an effect on the nervous system the capacities

TABLE 4

The action of temperature and humidity on muscles summarized. Duration of working period is expressed in minutes; total work performed in gram-millimeters

MUSCLE		TEMPERATURE AND HUMIDITY					
		Low		Intermediate		High	
		Duration	Work	Duration	Work	Duration	Work
Diaphragm	Average	148	147,957	151	124,325	142	117,317
	Percentage	100	100	102	84	96	79
Sartorius	Average	121	76,599	97	54,861	88	52,965
	Percentage	100	100	80	72	73	69
Extensor	Average	72	30,224	82	36,410	54	23,624
	Percentage	100	100	114	120	75	78
Average		113	84,927	110	71,865	101	64,635
Percentage		100	100	97	85	89	76

of the muscles themselves are diminished. Hence excessive muscular work, a whipping-up of the muscles, would tend toward earlier muscular exhaustion, and thus we have additional physiological justification for maintaining that with human beings who are obliged to labor in an atmosphere of extreme heat and humidity excessive and continuous muscular work should be avoided.

THE CONCENTRATION OF SUGAR IN THE BLOOD

As was indicated earlier in this paper, we had no reason to suspect that there is a necessary relationship between the working power of excised muscles and the concentration of the sugar in the blood.

Indeed, this portion of the work was begun as a continuation of the work previously reported by one of us (9) concerning the effect of common laboratory procedures upon the concentration of blood sugar. But the results seem to correlate very well with those obtained from a physical study of the muscles and hence to have a physiological significance.

The technique of conditioning and handling the animals and of collecting the samples of blood, and the method of analysis were the same as were described in the previous paper. The freedom with which the blood flows from the cut vessels of the neck varies considerably. In our experiments its collection was continued until the free flow ceased, and in practice it was found possible to determine this moment with approximate uniformity. The work of Scott, together with other data still unpublished, shows definitely that, at least when blood is collected from the cat by decapitation, the concentration of sugar decreases as the amount of blood drawn increases, so that the amount of blood drawn must be taken into consideration in the interpretation of results. In doing this 30 grams of blood per kilogram of body weight were taken as the standard and the calculation was made by the formula previously published. This formula is $y=b(x'-x)/a+y'$, in which a and b are constants and equal, respectively, 133 and 0.084, and x' represents the amount of blood drawn, y' its concentration of sugar in any one experiment, x the standard amount of blood per kilogram of body weight, and y the corresponding concentration of sugar.

Our results are presented in table 5. The dates of the experiments and the sex of the animals may be learned from the previous tables.

The first group of figures consists of the results obtained from the control series and show that simple confinement in the chamber is practically without effect when the series is considered as a whole. Thus, the averages for the actual and the calculated concentration of sugar are practically identical and vary but little from those of the standard series, 0.069 per cent, reported in the previous paper. It will be noted, however, that there is much more variation between the individuals of this series than was found for the standard animals. This of course necessitates a longer series than would otherwise be required if the conclusions drawn from such experiments are to be trusted.

Turning next to the last group of figures in table 5, we find among the results, after they have been calculated to 30 grams of blood per kilogram of body weight, but two in the series of twelve which exceed

TABLE 5

The action of temperature and humidity on the concentration of the sugar of the blood

NUMBER OF EXPERIMENT	NUMBER OF BLOOD SUGAR DETERMINATION	AVERAGE DRY BULB TEMPERATURE IN °C.	AVERAGE HUMIDITY IN PER CENT	BODY WEIGHT IN KG.	AMOUNT OF BLOOD DRAWN IN GRAMS PER KG. OF BODY WEIGHT	GRAMS OF GLUCOSE PER 100 GRAMS OF BLOOD		VARIATION FROM STANDARD OF 0.069 IN PER CENT OF STANDARD	
						Actual	Calculated for 20 gms. of blood per kg. of body weight	From actual concentration	From calculated concentration
Low temperature and humidity									
1	116	20.0	68	2.58	27.6	0.053	0.051	−23	−26
2	117	21.2	66	2.70	33.6	0.079	0.082	+15	+19
3	119	21.0	54	2.45	30.5	0.085	0.085	+23	+23
4	120	21.1	65	3.10	30.1	0.064	0.064	− 7	− 7
6	122	21.2	59	2.70	32.1	0.075	0.076	+ 9	+10
7	123	21.8	49	3.05	27.0	0.052	0.050	−25	−28
8	124	22.1	50	3.75	31.8	0.073	0.074	+ 6	+ 7
9	125	21.6	49	3.80	29.4	0.067	0.067	− 3	− 3
10	126	21.4	49	2.80	21.1	0.063	0.057	− 9	−17
Average		21.3	57	2.98	29.2	0.0679	0.0673	− 2	− 2
Percentage					100		100		
Intermediate temperature and humidity									
6	141	23.8	70	3.00	29.2	0.067	0.065	− 3	− 6
8	145	23.6	70	2.10	34.9	0.079	0.082	+15	+19
10	146	23.5	70	2.20	26.3	0.053	0.051	−23	−26
11	147	23.6	70	3.60	26.7	0.069	0.067	± 0	− 3
12	148	23.7	70	2.80	35.8	0.061	0.065	−12	− 6
Average		23.6	70	2.74	30.6	0.066	0.066	−4	−4
Percentage					105		98		
High temperature and humidity									
1	111	30.7	89	3.65	22.8	0.053	0.047	−23	−32
2	112	33.1	90	1.62	34.3	0.064	0.067	− 3	−17
3	113	35.0	94	3.78	18.5	0.065	0.058	− 6	−16
4	114	32.9	90	2.90	22.5	0.054	0.049	−22	−29
5	115	33.7	92	3.50	23.8	0.062	0.058	−10	−16
6	127	32.5	89	2.17	39.1	0.080	0.086	+16	+25
11	149	32.0	90	3.40	27.9	0.070	0.068	+ 1	− 1
12	150	32.4	87	2.80	24.6	0.061	0.058	− 1	−16
13	151	32.6	91	3.10	24.4	0.071	0.067	+ 3	− 3
14	152	32.2	96	3.01	32.1	0.060	0.061	−13	−12
15	153	32.6	89	3.70	27.4	0.078	0.076	+13	+10
16	154	32.8	95	3.50	25.3	0.062	0.059	−10	−14
Average		32.7	91	3.09	26.9	0.065	0.063	−6	−9
Percentage					92		94		

the standard of 0.069 per cent. And of these two one (Exp. 6), is so large that it leads one to suspect that some unrecognized factor has been imposed upon the animal. But, in spite of this, the average for the series 0.063, is well below that of the standard, and this fact, together with a tendency toward a low concentration of sugar, leads us to believe that this represents the typical condition of affairs when the animal is exposed to combined high temperature and high humidity. It will be noted also that the quantity of blood obtained is less—by 8 per cent—for these animals than for those of the control series. Whether or not this is indicative of a lessened vigor of the circulatory musculature, more or less similar to that shown for the skeletal muscles, or whether, as seems more probable, it is related to the cutaneous vasodilation that may be presumed to occur under the conditions to which the animals were subjected, we are not at present prepared to say.

Again, because the series is too short to warrant such conclusions, we are not prepared to attach significance to the intermediate concentration of sugar found in the blood of animals subjected to the intermediate conditions, as shown by the second group of figures in table 5. It is interesting to note, however, that the results as they stand are in exact harmony with those of the other two series on the basis of our interpretation.

We desire to call attention to the fact that we recognize that the depression of the concentration of blood sugar found by us is not great; in fact, it may possibly be considered by some persons as not beyond the range of experimental error. We believe, however, that such a contention is unjustified. In demanding extreme variations before significance is attached to them the physiologist must of necessity shut his eyes to many fundamental changes in physiological conditions. And, further, we would emphasize the fact that a lowering of the concentration of blood sugar is much more safely attributed to a given set of experimental conditions than is an increase of the concentration. This is because, as has been abundantly shown, many common factors cause a marked increase in the sugar, while comparatively few have been demonstrated to decrease it.

Any attempt to show the nature of the physiological significance of the lowered concentration of sugar found in animals exposed to conditions of high temperature and high humidity leads only into hypothesis, since many necessary data are not available. But it may not be amiss to call attention to the idea advanced by Cannon (10)

that the increased concentration of sugar in the blood of animals during intense emotions, together with the mechanism by which the increase is brought about, may be considered as a physiological adaptation. According to this idea the increased amount of sugar that frequently is present in the blood during an emotion is for the purpose of supplying the muscles with the increased energy required for the physical activity necessitated by the emotion. If there is, as this author thinks, a physiological adaptation of the fuel supplied to the increased amount of work to be done, it seems to us not unreasonable to believe that the reverse may also be true. In other words, when it is physiologically fitting that the animal reduce muscular exertion to a minimum, in order that the output of heat may be as low as possible, as in a hot and humid environment, the supply of fuel will be lowered correspondingly.

The complete proof of the hypothesis would require a calorimetric study of animals subjected to these conditions and, perhaps, especially a determination of respiratory quotients. It would also be of interest, in view of current theories of the mechanism of the mobilization of sugar, to determine the amount of adrenalin in the blood of these animals as compared with that of normal animals.

SUMMARY

Cats have been exposed for periods of six hours to atmospheric conditions varying only in respect to their temperature and their humidity. Three conditions have been studied, namely: a "low" condition, in which the average temperature was approximately 21°C. (69°F.) and the average humidity 52 per cent; an "intermediate" condition, in which the average temperature was 24°C. (75°F.) and the average humidity 70 per cent; and a "high" condition, in which the average temperature was 33°C. (91°F.) and the average humidity 90 per cent.

Muscles taken from the animals immediately after such exposure and stimulated to exhaustion show that the average duration of their working periods and the average total amounts of work performed decrease progressively in the three groups from the low, through the intermediate, to the high condition. Expressed in percentages the figures for the duration of working periods are: low 100, intermediate 97, high 89; those for the total amounts of work performed are: low 100, intermediate 85, high 76.

The degree of variability in the total amount of work performed by the muscles is less under the influence of the intermediate and the high atmospheric conditions, than under the low condition.

The amount of blood per kilogram of body weight that flows from the severed neck vessels on decapitation of animals subjected to similar exposures is less after the high than after the low condition. The percentage figures are: low 100, high 92.

The concentration of sugar in the blood of such animals decreases progressively in the three groups from the low, through the intermediate, to the high condition. The percentage figures are: low 100, intermediate 98, high 94.

It has been shown that under proper precautions cats confined in a small, well ventilated chamber may legitimately be used for experiments involving the determination of the sugar in the blood.

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